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=> s CRP complex
L1 575 CRP COMPLEX

=> s l1 and lipoproteins
L2 3 L1 AND LIPOPROTEINS

=> dup remove l2
PROCESSING COMPLETED FOR L2
L3 2 DUP REMOVE L2 (1 DUPLICATE REMOVED)

=> d l3 1-2 cbib abs

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
2003:931218 Document No. 140:788 C-reactive protein-binding ligands for the treatment and prevention of tissue damage. Pepys, Mark B.; Ley, Steven Victor; Cobb, Alexander John Andre (University College London, UK). PCT Int. Appl. WO 2003097104 A1 20031127, 78 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB2096 20030514. PRIORITY: GB 2002-11136 20020515.

AB The invention discloses an agent for use in medicine, comprising a plurality of ligands covalently co-linked so as to form a complex with a plurality of C-reactive protein (CRP) mols. in the presence thereof, wherein (i) at least two of the ligands are the same or different and are capable of being bound by ligand binding sites present on the CRP mols.; or (ii) at least one of the ligands is capable of being bound by a ligand binding site present on a CRP mol., and at least one other of the ligands is capable of being bound by a ligand binding site present on a serum

amyloid P component (SAP) mol. Preparation and inhibitory activity of 1,6-bis[(((trimethylammonium)ethoxy)phosphinyl)oxy]hexane (phosphocholine-hexane-phosphocholine) is described.

L3 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1
2002408846. PubMed ID: 12033985. Macrophage uptake of low-density lipoprotein bound to aggregated C-reactive protein: possible mechanism of foam-cell formation in atherosclerotic lesions. Fu Tao; Borensztajn Jayme. (Department of Pathology, Northwestern University Medical School, 303 East Chicago Avenue, Chicago, IL 60611, U.S.A.) Biochemical journal, (2002 Aug 15) 366 (Pt 1) 195-201. Journal code: 2984726R. ISSN: 0264-6021. Pub. country: England: United Kingdom. Language: English.

AB Foam cells found in atherosclerotic lesions are believed to derive from macrophages that take up aggregated low-density lipoprotein (LDL) particles bound to the extracellular matrix of arterial walls. C-reactive protein (CRP) is an acute-phase protein found in atherosclerotic lesions, which when immobilized on a solid phase, can bind and cluster LDL particles in a calcium-dependent manner. In the present study, we examined whether CRP-bound aggregated LDL could be taken up by macrophages in culture. CRP molecules were aggregated in the presence of calcium and immobilized on the surface of polystyrene microtitre wells. Human LDL added to the wells bound to and aggregated on the immobilized CRP, also in a calcium-dependent manner. On incubation with macrophages, the immobilized CRP-bound LDL aggregates were readily taken up by the cells, as demonstrated by immunofluorescence microscopy, by the cellular accumulation of cholesterol and by the overexpression of adipophilin. Immunofluorescence microscopy and flow-cytometry analysis established that the uptake of the LDL-**CRP complex** was not mediated by the CRP receptor CD32. These observations with immobilized CRP and LDL, approximating the conditions that exist in the extracellular matrix of the arterial wall, thus suggest that CRP may contribute to the formation of foam cells in atherosclerotic lesions by causing the aggregation of LDL molecules that are then taken up by macrophages through a CD32-independent pathway.

```
=> s c reactive protein complex
L4          50 C REACTIVE PROTEIN COMPLEX

=> s l4 and complex
L5          50 L4 AND COMPLEX

=> s l5 and LDL
L6           0 L5 AND LDL

=> s l5 and lipoproteins
L7           3 L5 AND LIPOPROTEINS

=> dup remove l7
PROCESSING COMPLETED FOR L7
L8           3 DUP REMOVE L7 (0 DUPLICATES REMOVED)

=> d l8 1-3 cbib abs

L8  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
1986:223434  Document No. 104:223434  CRP and neutrophils:  functional effects
    and complex uptake.  Shephard, Enid G.; Anderson, R.; Strachan,
    A. F.; Kuehn, S. H.; De Beer, F. C. (Fac. Med., Univ. Stellenbosch,
    Tygerberg, 7505, S. Afr.).  Clinical and Experimental Immunology, 63(3),
    718-27 (English) 1986.  CODEN: CEXIAL.  ISSN: 0009-9104.
AB  The uptake of C-reactive protein (CRP)-pneumococcal C-polysaccharide (CPS)
    complexes by human neutrophils was studied.  A specific CRP
    dependent mechanism of uptake was demonstrated.  This promoted CPS
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(complexed to CRP) clearance which was further enhanced by addnl. complement activation. Physiol. concns. of low-d. lipoprotein inhibited entry of complexed CPS into neutrophils but had no effect on entry of CRP alone. Pure human CRP had no effect on neutrophil chemotaxis and oxidative metabolism

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
1986:588782 Document No. 105:188782 Does human C-reactive protein circulate in complexed form? Equilibrium chromatography and dialysis studies. Pontet, M.; Tresca, J. P.; Ollivier, M.; Engler, R. (Fac. Med. St-Peres, Paris, 75270, Fr.). Marker Proteins in Inflammation, 3, 165-7 (English) 1986. CODEN: MPINEG.
AB Serum compds., particularly proteins in physiol. concns., can displace C-reactive protein (CRP)-phosphocholine binding, but it was not proved that circulating human CRP is in the complexed form.

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
1980:196134 Document No. 92:196134 Preparation and serum form of rabbit C-reactive proteins. Pontet, M.; Ayrault-Jarrier, M.; Burdin, J.; Gelin, M.; Engler, R. (Dep. Biochim., CNRS, Paris, 75270/06, Fr.). Biochimie, 61(11-12), 1293-9 (French) 1979. CODEN: BICMBE. ISSN: 0300-9084.
AB The preparation of rabbit C-reactive protein (CRP) involves a single-step affinity chromatog. This preparation takes advantage of the Ca-dependent affinity of CRP for an agarose gel bearing 2-aminoethanol dihydrogen-phosphate as a ligand. A prior chromatog. on agarose gel without the ligand allows the uptake of the serum amyloid P-component (SAP). The CRP, prepared according to this method, formed precipitating **complexes** in agarose with rabbit **lipoproteins**. The specificity of these interactions was studied. CRP-high-d. **lipoproteins** association produces a secondary precipitation arc when the pure CRP is revealed by a specific antiserum in agarose. Moreover, CRP in the serum is in the bound form only, and the binding involves low-d.-**lipoproteins** exclusively.

=> s haemostatic dysfunction diagnosis
L9 0 HAEMOSTATIC DYSFUNCTION DIAGNOSIS

=> s lipoprotein complex risk assesment
L10 0 LIPOPROTEIN COMPLEX RISK ASSESMENT

=> s acute phase protein complex
L11 1 ACUTE PHASE PROTEIN COMPLEX

=> d l11 cbib abs

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
2002:966970 Document No. 138:21824 Method for detecting a lipoprotein-**acute phase protein complex** and predicting an increased risk of system failure or mortality. Fischer, Timothy J.; Downey, Colin; Nesheim, Mike; Samis, John A.; Tejidor, Liliana; Toh, Cheng Hock; Walker, John B. (USA). U.S. Pat. Appl. Publ. US 2002193949 A1 20021219, 47 pp., Cont.-in-part of U. S. Ser. No. 591,642, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2001-19087 20011219. PRIORITY: US 1995-477839 19950607; US 1997-859773 19970521; US 1997-1647 19971231; US 1999-244340 19990204; US 2000-591642 20000609; WO 2001-US18611 20010608.
AB A method for diagnosing a condition of a patient involves the steps of (a) adding one or more reagents to a test sample from a patient, the test samples comprising at least part of a blood sample from the patient, in order to cause formation of a complex comprising at least one acute phase protein at least one human lipoprotein, while causing substantially no fiber polymerization; (b) measuring the formation of the complex over time so as

to derive a time-dependent measurement profile, and (c) determining a slope and/or total change in the time-dependent measurement profile, so as to diagnose a condition of the patient. A greater formation of the complex is correlated to increased probability of death of the patient.

```
=> s acute phase protein
L12       17217 ACUTE PHASE PROTEIN

=> s l12 and risk assesment
L13           0 L12 AND RISK ASSESMENT

=> s l12 and assesment
L14           0 L12 AND ASSESMENT

=> s l12 and complex
L15        1383 L12 AND COMPLEX

=> s l15 and lipoproteins
L16          35 L15 AND LIPOPROTEINS

=> dup remove l16
PROCESSING COMPLETED FOR L16
L17           26 DUP REMOVE L16 (9 DUPLICATES REMOVED)

=> d l17 1-26 cbib abs

L17  ANSWER 1 OF 26      MEDLINE on STN
2004079446.    PubMed ID: 14968563.   Development of blood examination method
     of serum amyloid A and LDL complex, and clinical application to
     prediction of cardiovascular event. Mashiba Shinichi; Ogasawara Ken;
     Takeya Motohiro; Wada Youichiro; Sahara Makoto; Kojima Shiho; Tabata
     Kazue; Ueda Masashi; Uchida Kazuo; Aizawa Tadanori; Kodama Tatsuhiko.
     (Kyoto Medical Science Laboratory, Kyoto 612-8486. ) Rinsho byori.
     Japanese journal of clinical pathology, (2004 Jan) 52 (1) 67-74.  Journal
     code: 2984781R. ISSN: 0047-1860. Pub. country: Japan. Language: Japanese.
AB   In recent years, it has been reported that the acute-
     phase proteins C-reactive protein(CRP) and serum amyloid
     A(SAA), the sera levels of which are elevated in inflammation, are also
     elevated in coronary artery disease such as acute myocardial infarction.
     Also, high-sensitivity CRP assay is thought to be useful in predicting the
     prognosis of coronary heart disease.  While investigating
     complexes of acute-phase proteins
     and low-density lipoprotein(LDL), we found a complex of LDL and
     SAA(SAA/LDL complex).  The SAA/LDL complex in blood
     are formed from LDL and HDL by an oxidation reaction.  Therefore, we
     developed an ELISA using anti-human SAA antibody and anti-human apoB, and
     determined a new method for measuring SAA/LDL complex in sera.
     We evaluated SAA/LDL complex as a new marker for prediction of
     prognosis in addition to the ordinary markers in consecutive 140 patients
     with stable coronary heart disease who had at least 1 coronary artery
     stenosis more than 50% in diameter at the diagnostic coronary angiography.
     Of these 140 patients, 2 developed fatal myocardial infarction, 2 cerebral
     infarction, and 17 angina pectoris requiring coronary revascularization
     therapy during 1 year and 6 months after blood examinations.  The SAA/LDL
     complex value in this EVENT group of 21 patients was significantly
     higher than that in the control group of 119 individuals.
     High-sensitivity CRP (hs-CRP) assay and SAA measurement showed no
     significant difference between the 2 groups.  The SAA/LDL complex
     reflects intravascular inflammation directly and can be a new marker more
     sensitive than hs-CRP or SAA for prediction of prognosis in patients with
     stable coronary artery disease.
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L17 ANSWER 2 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

2004013337 EMBASE Hyperlipoproteinemic low-density lipoprotein receptor-deficient mice are more susceptible to sepsis than corresponding wild-type mice. Lanza-Jacoby S.; Miller S.; Jacob S.; Heumann D.; Minchenko A.G.; Flynn J.T.. Dr. S. Lanza-Jacoby, Department of Surgery, Jefferson Medical College, 1025 Walnut Street, Philadelphia, PA 19107, United States. Susan.Lanza-Jacoby@mail.tju.edu. Journal of Endotoxin Research 9/6 (341-347) 2003.
Refs: 29.
ISSN: 0968-0519. CODEN: JENREB. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB High circulating concentrations of **lipoproteins** have been shown to modify the cytokine response and reduce mortality after endotoxin or live bacterial challenge. Sepsis, however, is more **complex** than endotoxemia, and it is not clear whether elevated plasma **lipoproteins;** will be protective. Previous studies have shown that the low-density-lipoprotein receptor deficient (LDLR(-/-)) mice with increased circulating LDL are protected against the lethal effects of endotoxemia and Gram-negative infection. We evaluated whether the LDLR(-/-) mice would be protected against the effects of sepsis induced by cecal ligation and puncture (CLP). Mortality was greater in LDLR(-/-) mice than in control C57B1/6J mice. At 120 h after inducing sepsis, 20% of the control mice survived whereas none of the LDLR(-/-) mice were alive. Prior to inducing sepsis, serum concentrations of amyloid A protein and lipopolysaccharide binding protein (LBP) were significantly elevated in the LDLR(-/-) mice in comparison to the C57B1/6J mice. Protein expression of sCD14 was also greater in the serum from the LDLR(-/-) mice than the C57B1/6J mice. The elevated serum concentrations of LBP and CD14 were not associated with increases in the levels of liver CD14 mRNA and LBP mRNA. After inducing sepsis, serum concentration of interleukin (IL)-1β was also significantly higher in LDLR(-/-) mice than in the control C57B1/6J mice. These findings indicate that the LDLR(-/-) mice were more susceptible to the lethal effects of sepsis induced by CLP. The LDLR(-/-) mice also had higher serum concentrations of baseline, acute phase response proteins, SAA and LBP, and increased production of IL-1β in response to CLP.

L17 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

2002:966970 Document No. 138:21824 Method for detecting a lipoprotein-**acute phase protein complex** and predicting an increased risk of system failure or mortality. Fischer, Timothy J.; Downey, Colin; Nesheim, Mike; Samis, John A.; Tejidor, Liliana; Toh, Cheng Hock; Walker, John B. (USA). U.S. Pat. Appl. Publ. US 2002193949 A1 20021219, 47 pp., Cont.-in-part of U. S. Ser. No. 591,642, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2001-19087 20011219. PRIORITY: US 1995-477839 19950607; US 1997-859773 19970521; US 1997-1647 19971231; US 1999-244340 19990204; US 2000-591642 20000609; WO 2001-US18611 20010608.

AB A method for diagnosing a condition of a patient involves the steps of (a) adding one or more reagents to a test sample from a patient, the test samples comprising at least part of a blood sample from the patient, in order to cause formation of a **complex** comprising at least one **acute phase protein** at least one human lipoprotein, while causing substantially no fiber polymerization; (b) measuring the formation of the **complex** over time so as to derive a time-dependent measurement profile, and (c) determining a slope and/or total change in the time-dependent measurement profile, so as to diagnose a condition of the patient. A greater formation of the **complex** is correlated to increased probability of death of the patient.

L17 ANSWER 4 OF 26 MEDLINE on STN DUPLICATE 1

2002408846. PubMed ID: 12033985. Macrophage uptake of low-density

lipoprotein bound to aggregated C-reactive protein: possible mechanism of foam-cell formation in atherosclerotic lesions. Fu Tao; Borensztajn Jayme. (Department of Pathology, Northwestern University Medical School, 303 East Chicago Avenue, Chicago, IL 60611, U.S.A.) Biochemical journal, (2002 Aug 15) 366 (Pt 1) 195-201. Journal code: 2984726R. ISSN: 0264-6021. Pub. country: England: United Kingdom. Language: English.

AB Foam cells found in atherosclerotic lesions are believed to derive from macrophages that take up aggregated low-density lipoprotein (LDL) particles bound to the extracellular matrix of arterial walls. C-reactive protein (CRP) is an **acute-phase protein** found in atherosclerotic lesions, which when immobilized on a solid phase, can bind and cluster LDL particles in a calcium-dependent manner. In the present study, we examined whether CRP-bound aggregated LDL could be taken up by macrophages in culture. CRP molecules were aggregated in the presence of calcium and immobilized on the surface of polystyrene microtitre wells. Human LDL added to the wells bound to and aggregated on the immobilized CRP, also in a calcium-dependent manner. On incubation with macrophages, the immobilized CRP-bound LDL aggregates were readily taken up by the cells, as demonstrated by immunofluorescence microscopy, by the cellular accumulation of cholesterol and by the overexpression of adipophilin. Immunofluorescence microscopy and flow-cytometry analysis established that the uptake of the LDL-CRP **complex** was not mediated by the CRP receptor CD32. These observations with immobilized CRP and LDL, approximating the conditions that exist in the extracellular matrix of the arterial wall, thus suggest that CRP may contribute to the formation of foam cells in atherosclerotic lesions by causing the aggregation of LDL molecules that are then taken up by macrophages through a CD32-independent pathway.

L17 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

2001:338762 Document No. 134:362292 Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile. Farr, Spencer (Phase-1 Molecular Toxicology, USA). PCT Int. Appl. WO 2001032928 A2 20010510, 222 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US30474 20001103. PRIORITY: US 1999-PV165398 19991105; US 2000-PV196571 20000411.

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

L17 ANSWER 6 OF 26 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
2001:899363 The Genuine Article (R) Number: BT11N. Fibrinogen biosynthesis - Assembly, intracellular degradation, and association with lipid synthesis and secretion. Redman C M (Reprint); Xia H. New York Blood Ctr, Lindsley F Kimball Res Inst, 310 E 67 St, New York, NY 10021 USA (Reprint); New York Blood Ctr, Lindsley F Kimball Res Inst, New York, NY 10021 USA. FIBRINOGEN (NOV 2001) Vol. 936, pp. 480-495. Publisher: NEW YORK ACAD SCIENCES. 2 EAST 63RD ST, NEW YORK, NY 10021 USA. ISSN: 0077-8923. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Plasma fibrinogen is synthesized primarily in hepatocytes and assembly of the three component chains (A alpha, B beta, and gamma) into its final form as a six-chain dimer (A alpha, B beta, gamma)(2) occurs rapidly in the lumen of the endoplasmic reticulum (ER). Assembly takes place in a stepwise manner with single chains interacting with each other to form A alpha-gamma and B beta-gamma **complexes**. The two-chain **complexes** then acquire another chain to form half-molecules (A alpha, B beta, gamma)(1), which in a final step are linked to form the six-chain (A alpha, B beta, gamma)(2) **complex**. As with other secreted glycoproteins, N-linked glycosylation of B beta and gamma chains commences in the ER and is completed in Golgi organelles. Sulfation and phosphorylation occur at post ER stages of the secretory process. Since some ER chaperones coisolate with nascent fibrinogen chains they have been implicated in assisting chain assembly. Studies with recombinant systems, using deletion and substitution mutants, indicate that initial chain assembly depends on hydrophobic interactions present in the C-terminal half of the coil-coil domains and that inter- and intra-disulfide bonds that stabilize fibrinogen are needed to complete chain assembly. Not all the chains that are synthesized are assembled into fibrinogen and the unassembled chains are not secreted. HepG2 cells contain surplus A alpha and gamma chains that accumulate as free gamma chains and as an A alpha-gamma **complex**. A alpha-gamma is degraded by lysosomes whereas the gamma chain is degraded by the proteasome-ubiquitin system. Studies with expression of single chains by COS cells confirm that gamma and B beta are hydrolyzed by proteasomes and indicate that Act is degraded partially both by lysosomes and proteasomes. The role of surplus chains in regulating fibrinogen assembly is not understood but overexpression of any one chain, elicited by transfection of HepG2 cells, results in the upregulation of the other two genes, increased fibrinogen synthesis and secretion, and maintenance of surplus intracellular A alpha and gamma chains. HepG2 cells, programmed in this manner to increase basal fibrinogen expression, have higher HMG-CoA reductase mRNA levels, enhanced cholesterol and cholesterol ester synthesis, and increased secretion of apolipoprotein B (apoB). Overexpression of basal levels of fibrinogen does not affect synthesis of other **acute phase proteins**. Enhanced secretion of apoB is due to diminished degradation of nascent apoB by proteasomes and not to increased expression. Increased secretion of apoB is associated with increased basal expression of fibrinogen and is not affected when fibrinogen expression is stimulated by interleukin-6. In HepG2 cells, a feedback mechanism exists and extracellular sterols specifically downregulate expression of the three fibrinogen genes. These studies link, at the cellular level, basal fibrinogen expression with lipid metabolism.

L17 ANSWER 7 OF 26 MEDLINE on STN DUPLICATE 2
2001560940. PubMed ID: 11606222. Activity of human trypanosome lytic factor in mice. Barker C; Barbour K W; Berger F G; Hajduk S L. (Department of Biochemistry and Molecular Genetics, School of Medicine, University of Alabama at Birmingham, Birmingham, AL 35394, USA.) Molecular and biochemical parasitology, (2001 Oct) 117 (2) 129-36. Journal code: 8006324. ISSN: 0166-6851. Pub. country: Netherlands. Language: English.

AB The inability of the cattle pathogen Trypanosoma brucei brucei to infect humans is due to an innate factor in human serum termed Trypanosome Lytic

Factor (TLF). Human haptoglobin-related protein is the proposed toxin in TLF and can exist either as a component of a minor subclass of high-density lipoprotein (TLF-1) or as a lipid free, high molecular weight protein **complex** (TLF-2). The trypanolytic activity of both TLF-1 and TLF-2 has been studied in vitro but their relative contributions to protection against T. b. brucei infection in vivo has not been established. In the present studies we show that treatment of T. b. brucei infected mice with TLF-1 resulted in a dose dependent decrease in parasite numbers but did not affect parasite numbers in mice infected with Trypanosoma brucei rhodesiense, the causative agent of the human sleeping sickness. Similarly, pretreatment of mice with TLF-1 resulted in protection against a challenge by T. b. brucei but had no effect on T. b. rhodesiense challenge. Induction of the **acute phase protein** haptoglobin, a natural antagonist of TLF-1, diminished but did not abolish the protection against trypanosome challenge. In addition, haptoglobin knockout mice showed higher levels of TLF-1 mediated protection against a T. b. brucei challenge. These results suggest that while TLF-1 is active in vivo, even in the presence of elevated levels of haptoglobin, its activity is modulated in a dose dependent fashion by haptoglobin in the circulation.

L17 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
2000:135485 Document No. 132:306072 Acute phase serum amyloid A protein increases high density lipoprotein binding to human peripheral blood mononuclear cells and an endothelial cell line. Hayat, S.; Raynes, J. G. (Immunology Unit, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, WC1E 7HT, UK). Scandinavian Journal of Immunology, 51(2), 141-146 (English) 2000. CODEN: SJIMAX. ISSN: 0300-9475. Publisher: Blackwell Science Ltd..
AB Serum Amyloid A (SAA) is an **acute-phase protein** secreted mainly by hepatocytes and is largely associated with high-d. lipoprotein (HDL) in plasma. It has been suggested that SAA alters HDL binding to the cell surface and that this in turn changes HDL-mediated cholesterol delivery to cells. Incorporation of SAA into HDL at concns. equivalent to those found physiol. in moderate inflammation mediated a 1.5-fold increase in the binding of HDL to adherent peripheral blood mononuclear cells but had no effect on binding of the lipoprotein to the monocyte cell lines, U937 or THP-1. SAA incorporation also increased binding to an endothelial cell line, EA.hy.926. Hepatoma cells (HuH-7) showed no change in specific binding of the SAA-enriched HDL particle compared to normal HDL. These results suggest that a specific receptor for HDL-bound SAA is found on differentiated human macrophages and an endothelial cell line, which may have functional significance in lipid metabolism or other macrophage responses during inflammation.

L17 ANSWER 9 OF 26 MEDLINE on STN
2001070132. PubMed ID: 11111225. Acute phase markers are associated with reduced plasma lipid levels in a population of hospitalized elderly patients. Volpato S; Palmieri E; Fellin R; Zuliani G. (Department of Clinical and Experimental Medicine, Section of Internal Medicine II, University of Ferrara, Italy.) Gerontology, (2000 Jan-Feb) 46 (1) 22-7. Journal code: 7601655. ISSN: 0304-324X. Pub. country: Switzerland. Language: English.
AB BACKGROUND: Several epidemiological studies have documented the presence of a 'J' or 'U' association between total cholesterol levels and total mortality. Not only the mechanism underlying the association between increased mortality and low total cholesterol values is not completely clear, but the relationship itself also appears to be **complex** in the elderly. OBJECTIVE: The aim of the study was to evaluate the possible association between some biohumoral markers of the acute phase, comorbidity, disability, and reduced levels of some lipoprotein parameters in a sample of hospitalized elderly subjects. METHODS: 341 patients over 65 years of age (185 males, 156 females; mean age 76.2 years),

consecutively admitted to our department from 1994 to 1995, were studied. Acute phase was defined as the simultaneous presence of: (1) increased alpha2-plasma protein on electrophoresis (>12%); (2) high fibrinogen concentration (>450 mg/dl), and (3) increased blood sedimentation rate (>15 and >20 mm 1 h in males and females, respectively). RESULTS: The prevalence of signs of acute phase was higher in males and in the youngest patients, but did not change with the level of comorbidity. Patients with signs of acute phase were characterized by lower total, low-density lipoprotein (LDL)- and high-density lipoprotein (HDL)-cholesterol levels compared to subjects without signs of acute phase; this difference was significant even after adjustment for indicators of comorbidity, disability, and nutritional status. Multivariate logistic regression analysis evidenced that the simultaneous presence of these three markers of acute phase was independently associated with low levels of total cholesterol [odds ratio (OR) 2.1, 95% confidence interval (CI) 1.1 - 3.9], and HDL-cholesterol (OR 2.3, 95% CI 1.2 - 4.2), considered as the sex-specific first quintile. CONCLUSION: The findings of this study demonstrate an independent association between acute phase markers and low levels of total and HDL-cholesterol, suggesting that recognized or subclinical diseases in elderly patients may determine a reduction in these plasma lipids. Low level of total and HDL-cholesterol should be considered as possible clinical markers of an underlying state of acute phase rather than a sign of malnutrition. Given the high prevalence of chronic diseases in the elderly, epidemiological studies addressing the lipid profile in this age group should take into account the possible confounding effect of the presence of signs of acute phase.

L17 ANSWER 10 OF 26 MEDLINE on STN
1999453164. PubMed ID: 10521363. Complement and atherogenesis: binding of CRP to degraded, nonoxidized LDL enhances complement activation. Bhakdi S; Torzewski M; Klouche M; Hemmes M. (Institute of Medical Microbiology and Hygiene, Johannes Gutenberg-University, Mainz, Germany.. makowiec@goofy.zdv.uni-mainz.de) . Arteriosclerosis, thrombosis, and vascular biology, (1999 Oct) 19 (10) 2348-54. Journal code: 9505803. ISSN: 1079-5642. Pub. country: United States. Language: English.

AB Complement activation occurs in temporal correlation with the subendothelial deposition of LDL during early atherogenesis, and complement also plays a pathogenetic role in promoting lesion progression. Two lesion components have been identified that may be responsible for complement activation. First, enzymatic degradation of LDL generates a derivative that can spontaneously activate complement, and enzymatically degraded LDL (E-LDL) has been detected in the lesions. Second, C-reactive protein (CRP) colocalizes with complement C5b-9, as evidenced by immunohistological studies of early atherosclerotic lesions, so the possibility exists that this **acute phase protein** also fulfills a complement-activating function. Here, we report that addition of LDL and CRP to human serum did not result in significant C3 turnover. Addition of E-LDL provoked complement activation, which was markedly enhanced by CRP. Binding of CRP to E-LDL was demonstrated by sucrose flotation experiments. Binding was Ca(2+)-dependent and inhibitable by phosphorylcholine, and the complement-activating property of E-LDL was destroyed by treatment with phospholipase C. These results indicated that CRP binds to phosphorylcholine groups that become exposed in enzymatically degraded LDL particles. Immunohistological studies complemented these findings in showing that CRP colocalizes with E-LDL in early human atherosclerotic lesions. Thus enzymatic, nonoxidative modification of tissue-deposited LDL can be expected to confer CRP-binding capacity onto the molecule. The ensuing enhancement of complement activation may be relevant to the development and progression of the atherosclerotic lesion.

L17 ANSWER 11 OF 26 MEDLINE on STN DUPLICATE 3
1998414158. PubMed ID: 9743226. C-reactive protein frequently colocalizes

with the terminal complement **complex** in the intima of early atherosclerotic lesions of human coronary arteries. Torzewski J; Torzewski M; Bowyer D E; Frohlich M; Koenig W; Waltenberger J; Fitzsimmons C; Hombach V. (Department of Cardiology, University of Ulm, Germany.) Arteriosclerosis, thrombosis, and vascular biology, (1998 Sep) 18 (9) 1386-92. Journal code: 9505803. ISSN: 1079-5642. Pub. country: United States. Language: English.

AB There is increasing evidence that complement activation may play a role in atherogenesis. Complement proteins have been demonstrated to be present in early atherosclerotic lesions of animals and humans, and cholesterol-induced atherosclerotic lesion formation is reduced in complement-deficient animals. Potential complement activators in atherosclerotic lesions are now a subject matter of debate. C-reactive protein (CRP) is an **acute-phase protein** that is involved in inflammatory processes in numerous ways. It binds to **lipoproteins** and activates the complement system via the classic pathway. In this study we have investigated early atherosclerotic lesions of human coronary arteries by means of immunohistochemical staining. We demonstrate here that CRP deposits in the arterial wall in early atherosclerotic lesions with 2 predominant manifestations. First, there is a diffuse rather than a focal deposition in the deep fibroelastic layer and in the fibromuscular layer of the intima adjacent to the media. In this location, CRP frequently colocalizes with the terminal complement **complex**. Second, the majority of foam cells below the endothelium show positive staining for CRP. In this location, no colocalization with the terminal complement proteins can be observed. Our data suggest that CRP may promote atherosclerotic lesion formation by activating the complement system and being involved in foam cell formation.

L17 ANSWER 12 OF 26 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

1998:341530 The Genuine Article (R) Number: ZK414. Chylomicrons alter the hepatic distribution and cellular response to endotoxin in rats. Harris H W (Reprint); Rockey D C; Chau P. UNIV CALIF SAN FRANCISCO, SAN FRANCISCO GEN HOSP, DEPT SURG, WARD 3A, 1001 PORTERO AVE, SAN FRANCISCO, CA 94110 (Reprint); DUKE UNIV, MED CTR, DEPT MED, DURHAM, NC 27710. HEPATOLOGY (MAY 1998) Vol. 27, No. 5, pp. 1341-1348. Publisher: W B SAUNDERS CO. INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0270-9139. Pub. country: USA. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Chylomicrons (CM) can bind endotoxin (lipopolysaccharide [LPS]), forming CM-LPS **complexes**, and protect against endotoxic shock and death in rodent models of gramnegative sepsis, The liver appears to play a central role in this process, as demonstrated by the increased uptake of LPS by this organ. We examined the effect of CM on the uptake and cellular response to injected I-125-LPS by hepatocytes and hepatic nonparenchymal cells. Whereas CM increased the uptake of LPS by both hepatocytes and Kupffer cells, the increase was proportionately greater in hepatocytes than Kupffer cells. Importantly, CM-LPS **complexes** inhibited inducible nitric oxide synthase (iNOS) mRNA expression and NO production in Kupffer cells and endothelial cells, reducing mRNA levels by 45% to 50% as compared with LPS alone. CM-bound LPS also reduced NO production by hepatocytes in response to cytokine stimulation. Lastly, CM-LPS **complexes** yielded a concentration-dependent inhibition of LPS-induced tumor necrosis factor alpha (TNF-alpha) production by Kupffer cells in vitro. These data indicate that the mechanism by which CM protect against endotoxicity may involve an increased uptake of LPS by hepatocytes. Moreover, uptake of CM-bound LPS by liver cells attenuates the capacity of these cells to respond to proinflammatory stimulation. These results highlight important anti-inflammatory properties of CM.

L17 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

1998:343512 Document No. 130:51263 Comparison of the binding and endocytosis of high-density lipoprotein from healthy (HDL) and inflamed (HDLSAA)

donors by murine macrophages of four different mouse strains. Rocken, C.; Kisilevsky, Robert (Queen's University and The Syl and Molly Apps Medical Research Centre, Department of Pathology, Kingston General Hospital, Kingston, ON, K7L 3N6, Can.). Virchows Archiv, 432(6), 547-555 (English) 1998. CODEN: VARCEM. ISSN: 0945-6317. Publisher: Springer-Verlag.

AB Serum amyloid A (SAA) is a plasma **acute phase protein** and the precursor of the AA-fibril protein deposited in AA-amyloidosis. SAA is bound mainly to high-d. **lipoproteins** (HDLSAA). Previous investigations have demonstrated that peritoneal macrophages (mϕ) from mice are capable of binding and endocytosing HDLSAA. This observation may indicate a pathway by which SAA enters the mϕ and where its intracellular metabolism may be followed by degradation and/or amyloidogenesis. Since binding and internalization defects of **lipoproteins** may be associated with different diseases, it is possible that mouse strain susceptibility to amyloidosis is associated with qual. differences in the binding and internalization of HDLSAA. To test this hypothesis a series of binding and internalization expts. was performed in vitro with mO from four different mouse strains, CD-1, A/J, C57BL/6J and C3H/HeJ, which differ in their susceptibility to AA-amyloidosis. Using colloidal gold-labeled **lipoproteins**, it was evident by light and electron microscopy that mϕ from all four mouse strains are capable of binding and internalizing HDL (without SAA) and HDLSAA. HDL and HDLSAA were found in such compartments of the receptor-mediated pathway as coated pits, coated vesicles, endosomes and multivesicular bodies and in lipid droplets; no qual. differences were observed Therefore, it is unlikely that a defect in binding and uptake of HDLSAA is related to the different susceptibilities of these mouse strains to develop AA-amyloidosis. However, the results do not exclude the possibility that differences in the intracellular processing of SAA following endocytosis of HDLSAA is involved in this differing susceptibility.

L17 ANSWER 14 OF 26 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

1998:820483 The Genuine Article (R) Number: 130RH. Human serum amyloid A has cytokine-like properties. Patel H (Reprint); Fellowes R; Coade S; Woo P. UNIV COLL LONDON, SCH MED, DEPT MOL PATHOL, MRC, MOL RHEUMATOL GRP, WINDEYER BLDG, 46 CLEVELAND ST, LONDON W1P 6DB, ENGLAND (Reprint). SCANDINAVIAN JOURNAL OF IMMUNOLOGY (OCT 1998) Vol. 48, No. 4, pp. 410-418. Publisher: BLACKWELL SCIENCE LTD. P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND. ISSN: 0300-9475. Pub. country: ENGLAND. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Human serum amyloid A (SAA) proteins are a group of 12-14 kDa apolipoproteins found predominantly in the high-density lipoprotein (HDL) fraction of plasma. Several functions have been proposed for SAA, but its primary physiological function remains elusive. In this report, we used the monocytic cell line THP-1 to investigate whether recombinant SAA1 (rSAA) or the HDL-rSAA protein **complex** can affect the capacity of these cells to produce inflammatory cytokines in vitro. Incubation of rSAA, plasma HDL (which contains less than or equal to 30 mu g/ml of SAA) or HDL-rSAA **complex** with THP-I cells induced synthesis of IL-1 beta, IL-1ra and sTNFR-II protein and mRNA. The induction of cytokine synthesis was not due to endotoxin contamination since the effect was abrogated by protein denaturation. The rSAA and HDL-rSAA **complex** did not induce detectable levels of IL-6 or TNF alpha protein or mRNA. In contrast 10 mu g/ml LPS stimulated secretion of the inflammatory cytokines, IL-1 beta, IL-6 and TNF alpha, as well as IL-1ra and sTNFR-II from THP-1 cells. We confirmed that rSAA has chemoattractant properties in vivo, by subcutaneous injections into mice: and examined the histology of the injection site at 72 h, however, the HDL-rSAA **complex** has a substantially reduced effect.

L17 ANSWER 15 OF 26 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

DUPLICATE 4

1999007285 EMBASE [Cellular systems implicated in production of free radicals and physiological functions of these radicals and free radicals in human pathology]. RADICAUX LIBRES ET ANTI-OXYDANTS : PHYSIOLOGIE, PATHOLOGIE HUMAINE ET ASPECTS THERAPEUTIQUES (ILEME PARTIE). Sahnoun Z.; Jamoussi K.; Zeghal K.M.. Z. Sahnoun, Laboratoire de Pharmacologie, Faculte de Medecine, 3029 Sfax, Tunisia. Therapie 53/4 (315-339) 1998.
Refs: 183.
ISSN: 0040-5957. CODEN: THERAP. Pub. Country: United Kingdom. Language: French. Summary Language: French; English.

AB Although they are considered as destructive agents, free radicals can sometimes become useful. Their presence is intimately coupled with the activity of certain hemal oxydases which insert an atom of oxygen into their substrate by a stereospecific radical mecanism. The cytochromes P450 and the enzymes of the eicosanoide metabolism are some examples. The free radicals can act as second cellular messengers, especially to modulate the metabolism of arachidonic acid and the prostaglandin tract or to infer a myorelaxation. They can even play the role of neurotransmitters such as azote monoxyde. The activation of phagocytes, which is an essential event in the inflammatory reaction, integrates these notions at several levels: in the mechanisms of bacterial death, in the spread of the inflammatory reaction and in the alteration of the extra-cellular matrix. The inflammatory reaction is initiated by interactions between vascular endothelium, platelets and leukocytes including signal exhanges, adhesion molecule expression and secretion of chimiotactic mediators. Activation of vascular endothelium is a key event in the initiation of the phenomenon. The cells intervening in the precocious inflammatory phase were tissular mastocytes and platelet-liberating mediators (histamine) and neutrophile cells responsible for vascular injuries induced by oxygen free radicals and nitric oxide. Reactive oxygen intermediates play a critical role, primarily to limit tissue damage and prevent or inhibit infection, secondary to enhancing and prolonging reaction. The monocytes and platelets liberate cytokines early, which appears to be important in activation and production of an inflammatory response. In fact, cytokines, especially TNFα and IL-1, induce synthesis and secretion endothelial adhesion molecules such as ICAM-1, VCAM-1 and E-selectin, which have been demonstrated to mediate leukocyte recruitment to sites of inflammation. The cytokines also activate the fibroblasts and endothelial cells that produce, among others, free radicals and other chimiotactic cytokines of which some (IL-8 and related) can induce neutrophil degranulation and stimulate oxidative stress and formation of free radicals. Furthermore, endothelial cells have been shown to make use of a broad repertoire of cytokines including IL-1, IL-6, IL-8, MCP-1 and gro/MGSA, which may be secreted during an inflammatory response and exercise pro-inflammatory functions. Under the influence of the inflammatory mediators, other enzymes are also activated. The inducible isoforms of cycloxygenase (COX-2) and nitric oxide synthase (iNOS) play an important role in inflammatory reactions via the production respectively of prostaglandins and nitric oxide. The induction of cell adhesion molecules (ICAM-1, VCAM-1 and E-selectin), cytokines, **acute phase proteins**, growth factors, COX-2 and iNOS expression is mediated by the activation of transcriptional factors, especially the nuclear factor kappa B (NF-κB). The NF-κB system is essentially involved in immediate early expression of various immunoregulatory genes and has been demonstrated to represent an important regulatory system of endothelial activation. The target genes for NF-κB comprise a growing list of genes intrinsically linked to a coordinated inflammatory response. The NF-κB is a heterodimer composed of two subunits (p65 and p50). In non-stimulated cells, NF-κB resides in the cytoplasm as an inactive **complex** bound to its inhibitor, IκB. Upon stimulation with various agents including cytokines, mitogenes, viruses and reactive oxygen intermediates, IκB dissociates from the NF-κB-IκB **complex** and translocates to the nucleus, binding with high affinity to specific sites in the promoter regions of target genes and

stimulating their transcription. In the case of any weakness of this anti-oxidizing defence or any over-production of radical species, a state of oxidative stress occurs. These radical species, without control, will damage different biological targets: lipids, DNA and proteins. Disturbances of the cellular metabolism will be the result, unless some reparation systems intervene. However, these radical species are the subject of increasing interest mainly because it is assumed that they will take part in the physiopathological mechanisms in different human diseases. Their incrimination in the atherosclerotic process, in carcinogenesis and in paraquat poisoning in itself justifies this interest. In the atherogenic cascade, the primum movens will be the oxidization of the lipoprotein particles of low density (LDL) in the vascular intima. These modified LDL will be recognized by the 'scavenger' receivers of the macrophages, then phagocytes. This non-stop phenomenon will lead to foam cells, then to lipidic streaks. The cytoxicity of those oxidized **lipoproteins** contributes to the formation of the lipidic nucleus of atheroma. The oxidized LDL, through their chemotactic mitogen properties, their immunogenicity and its activator effect of NF-κB, in association with reactive oxygen intermediates, will exacerbate the inflammatory reaction which accompanies the atheroma plaque. Moreover, the enrichment in vitro of LDL with anti-oxidants (for example α-tocopherol) enables reduction of the susceptibility of these particles to oxidization. Those observations have aroused researchers' curiosity in the direction of new therapeutic or preventive possibilities for atherosclerosis. The free radicals can also behave as mediators for carcinogenesis. In fact, they have shown, in vitro, their capacity to induce certain changes in the structure of DNA, to activate certain transduction circuits or to modulate the activity of genes. Thus they may take part in the tumoral initiation by their mutagenic power, by activation of proto-oncogenes or by the inhibition of tumour-removing genes.

L17 ANSWER 16 OF 26 MEDLINE on STN

95307189. PubMed ID: 7540449. [Immunochemical studies of several proteins in angina pectoris]. Immunokhimicheskie issledovaniia nekotorykh belkov pri stenokardii. Kovalenko E V; Petrunin D D. Vestnik Rossiiskoi akademii meditsinskikh nauk / Rossiiskaia akademiia meditsinskikh nauk, (1995) (3) 45-7. Journal code: 9215641. ISSN: 0869-6047. Pub. country: RUSSIA: Russian Federation. Language: Russian.

AB A comprehensive immunochemical assay was developed for quantification of apoproteins of the atherogenic **lipoproteins** B, H, Lp(a) and the "**acute phase proteins**" with unstable angina pectoris that had varied increases in the parameters studied in comparison with their physiological measures. The significance of the proteins under test was discussed in terms of pathogenesis of atherosclerosis. The asset of a **complex** immunochemical assay as part of the procedure involved simplicity and accessibility for wide medical practice, providing valid information.

L17 ANSWER 17 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

1995:341496 Document No.: PREV199598355796. Immunochemical studies of some proteins in angina pectoris. Kovalenko, E. V.; Petrunin, D. D.. Res. Inst. Phys.-Chem. Med., Russ. Minist. Health Med. Ind., Moscow, Russia. Vestnik Rossiiskoi Akademii Meditsinskikh Nauk, (1995) Vol. 0, No. 3, pp. 45-47. Language: Russian.

AB A comprehensive immunochemical assay was developed for quantification of apoproteins of the atherogenic **lipoproteins** B, H, Lp(a) and the "**acute phase proteins**" with unstable angina pectoris that had varied increases in the parameters studied in comparison with their physiological measures. The significance of the proteins under test was discussed in terms of pathogenesis of atherosclerosis. The asset of a **complex** immunochemical assay as part of the procedure involved simplicity and accessibility for wide medical practice, providing

valid information.

L17 ANSWER 18 OF 26 MEDLINE on STN DUPLICATE 5
94216492. PubMed ID: 8163654. Intact human ceruloplasmin oxidatively modifies low density lipoprotein. Ehrenwald E; Chisolm G M; Fox P L. (Department of Cell Biology, Cleveland Clinic Research Institute, Ohio 44195.) Journal of clinical investigation, (1994 Apr) 93 (4) 1493-501. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB Ceruloplasmin is a plasma protein that carries most of the copper found in the blood. Although its elevation after inflammation and trauma has led to its classification as an **acute phase protein**, its physiological role is uncertain. A frequently reported activity of ceruloplasmin is its ability to suppress oxidation of lipids. In light of the intense recent interest in the oxidation of plasma LDL, we investigated the effects of ceruloplasmin on the oxidation of this lipoprotein. In contrast to our expectations, highly purified, undegraded human ceruloplasmin enhanced rather than suppressed copper ion-mediated oxidation of LDL. Ceruloplasmin increased the oxidative modification of LDL as measured by thiobarbituric acid-reacting substances by at least 25-fold in 20 h, and increased electrophoretic mobility, conjugated dienes, and total lipid peroxides. In contrast, ceruloplasmin that was degraded to a **complex** containing 115- and 19-kD fragments inhibited cupric ion oxidation of LDL, as did commercial preparations, which were also degraded. However, the antioxidant capability of degraded ceruloplasmin in this system was similar to that of other proteins, including albumin. The copper in ceruloplasmin responsible for oxidant activity was not removed by ultrafiltration, indicating a tight association. Treatment of ceruloplasmin with Chelex-100 removed one of seven copper atoms per molecule and completely blocked oxidant activity. Restoration of the copper to ceruloplasmin also restored oxidant activity. These data indicate that ceruloplasmin, depending on the integrity of its structure and its bound copper, can exert a potent oxidant rather than antioxidant action on LDL. Our results invite speculation that ceruloplasmin may be in part responsible for oxidation of LDL in blood or in the arterial wall and may thus have a physiological role that is quite distinct from what is commonly believed.

L17 ANSWER 19 OF 26 MEDLINE on STN
93316919. PubMed ID: 8326923. Cytokine mediators of malnutrition: clinical implications. Hardin T C. Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition, (1993 Apr) 8 (2) 55-9. Ref: 63. Journal code: 8606733. ISSN: 0884-5336. Pub. country: United States. Language: English.

AB During the past decade, the relationships that exist between inflammatory cytokines and the metabolic changes associated with critical illness have been the focus of extensive research efforts. Alterations in protein metabolism, characterized by increased peripheral protein catabolism and increased hepatic synthesis of **acute-phase proteins**, have been reported with tumor necrosis factor, interleukin-1, and interleukin-6 administration in animals and humans. Hyperlipoproteinemia has also been observed, particularly in association with increases in very-low-density **lipoproteins** and hepatic fatty acid synthesis. The release of counter-regulatory hormones in response to cytokine activity contributes to these metabolic changes as well. An understanding of the **complex** interactions of cytokines as mediators of intermediary metabolism is important to clinicians caring for critically ill patients.

L17 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
1993:122292 Document No. 118:122292 Acute-phase plasma protein response to cholera intoxication in healthy and diabetic rats. Fouad, Fouad Mounir; Marshall, William D.; Farrell, Patrick G.; FitzGerald, Sian (Dep. Food

Sci. Agric. Chem., McGill Univ., QC, Can.). Journal of Toxicology and Environmental Health, 38(1), 1-18 (English) 1993. CODEN: JTEHD6. ISSN: 0098-4108.

AB The aim of the present study is twofold: to establish the response of hepatic machinery of plasma protein biosynthesis to cholera intoxication, and to examine the same response of alloxan-diabetic hepatocytes with minimal capacity of synthesis of plasma proteins. Direct lesion of hepatic plasma membranes via i.p. administration of cholera toxin to male rats resulted in a typical acute-phase response (APR) of plasma proteins, which had regressed to levels similar to those of health controls approx. at 240 h postintoxication. The d 2 response to a single 0.16 mg/kg body weight dose was typified by a 23% reduction in the level of albumin, but a 6-

and

24-fold increase in the levels of fibrinogen and alpha-1-acid glycoproteins, resp. This response was similar (in direction but not in magnitude) to the acute-phase reaction to a simple s.c. administration of carrageenan. The intoxication was accompanied by a massive leakage, into the peritoneal cavity, of plasma fluid, which embraced the complete profile of acute-phase reactants. A three-step mechanism is proposed to account for the observations as follows: firstly, there is rapid formation of a stable **complex** between subunit B of the toxin and ganglioside GM1 of hepatic plasma membrane. An APR is induced in response to the alteration(s) of hepatic plasma membranes. Secondly, the release, from the choleragen-membrane **complex**, of polypeptide A1 and its subsequent penetration of the hepatic membrane result in both activation of adenylate cyclase and increased vascular permeability of hepatic membranes. This leads, in turn, to exudation of components of plasma fluid in the peritoneal cavity of intoxicated rats. An alternate rationale for this exudation is the slow leakage of plasma proteins out of the blood vascular system (possibly through microvesicles) into the peritoneal cavity of cholera intoxicated rats. The spectrum of acute-phase hepatic secretory components were mirrored in the corresponding peritoneal exudate. Thirdly, the increased hepatic membrane flow provides the continued renewal of plasma membrane proteins required for its eventual repair by either endocytosis or sloughing off the toxin-bound membrane segments into the circulatory system, thus producing regression of APR. Livers of diabetic rats, an already established model in terms of APR, responded to i.p. administration of cholera toxin by increased biosynthesis of the identified plasma proteins and a marked reduction in total free-glucose in serum. Thus, innoculation of diabetic rats with cholera toxin resulted in the addition of the poorly controlled sugar residues onto polypeptide chains, a postribosomal process that is an alternative pathway for the metabolism of excess glucose.

L17 ANSWER 21 OF 26 MEDLINE on STN

92031356. PubMed ID: 1834167. Transient increase of plasma lipoprotein(a) in patients with unstable angina pectoris. Does lipoprotein(a) alter fibrinolysis?. Oshima S; Uchida K; Yasu T; Uno K; Nonogi H; Haze K. (Department of Internal Medicine, National Cardiovascular Center, Osaka, Japan.) Arteriosclerosis and thrombosis : a journal of vascular biology / American Heart Association, (1991 Nov-Dec) 11 (6) 1772-7. Journal code: 9101388. ISSN: 1049-8834. Pub. country: United States. Language: English.

AB It has been shown that lipoprotein(a) (Lp[a]) may interfere with the fibrinolytic system and that the Lp(a) level in an individual remains constant. To evaluate the effects of Lp(a) on the fibrinolytic system in patients with unstable angina, we measured plasma levels of Lp(a), the alpha 2-plasmin inhibitor-plasmin **complex**, and the thrombin-antithrombin III **complex**. The latter is a marker of thrombin generation, and the alpha 2-plasmin inhibitor-plasmin **complex** is an indicator of plasminogen activation. Venous plasma samples were taken from 18 patients with unstable angina and 18 patients with stable exertional angina who had been matched for clinical variables. On admission, plasma levels of Lp(a) were significantly higher in patients

with unstable angina than in those with stable exertional angina (319 +/- 193 mg/l versus 191 +/- 141 mg/l, respectively; p less than 0.05). On admission, plasma levels of the alpha 2-plasmin inhibitor-plasmin **complex** and of the thrombin-antithrombin III **complex** were also significantly higher in patients with unstable angina than in those with stable exertional angina (0.78 +/- 0.42 micrograms/ml and 3.6 +/- 1.3 ng/ml versus 0.41 +/- 0.13 micrograms/ml and 1.9 +/- 0.5 ng/ml, respectively; p less than 0.01). In nine of the 18 patients with unstable angina, serial changes of plasma levels of Lp(a), the alpha 2-plasmin inhibitor-plasmin **complex**, the thrombin-antithrombin III **complex**, and the **acute-phase proteins** C-reactive protein and alpha 1-antitrypsin were examined for 3 weeks after admission.(ABSTRACT TRUNCATED AT 250 WORDS)

L17 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
1987:131708 Document No. 106:131708 **Acute phase protein** modulating endotoxic activity of lipopolysaccharides, compositions and methods. Ulevitch, Richard J.; Tobias, Peter S. (Scripps Clinic and Research Foundation, USA). PCT Int. Appl. WO 8606279 A1 19861106, 90 pp. DESIGNATED STATES: W: JP, US; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1986-US936 19860428. PRIORITY: US 1985-728833 19850430.

AB An α2,β1-glycoprotein (mol. weight about 60,000), isolated from acute-phase serum and designated lipopolysaccharide-binding protein (LBP), is administered into the blood stream of an animal host subject to infection by gram-neg. bacteria which secrete lipopolysaccharide (LPS) to alleviate the toxic effects of LPS. LBP retards the binding of LPS to high-d. lipoprotein in the host's serum. Labeled LBP is useful as a reagent for detection of LPS in the serum by **complex** formation. A synthetic peptide comprising all or part of the first 39 N-terminal amino acids of rabbit LBP is linked to an immunogenic carrier and used to prepare antibodies to LBP for use in immunoassays for LBP.

L17 ANSWER 23 OF 26 MEDLINE on STN
86049279. PubMed ID: 2415051. Soluble immune **complexes**, **acute phase proteins** and E-rosette inhibitory substance in sera of malnourished children. Salimonu L S. Annals of tropical paediatrics, (1985 Sep) 5 (3) 137-41. Journal code: 8210625. ISSN: 0272-4936. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The percentage of circulating E-rosetting lymphocytes and the presence of serum E-rosette inhibitory substance were determined in 58 marasmic, 13 kwashiorkor and 22 well-fed children. The blood levels of soluble immune **complexes** and some **acute phase proteins** were also measured. The percentage of E-rosetting lymphocytes was significantly higher in the well-fed than in the malnourished children. The presence of the inhibitory substance in serum correlated with depressed levels of circulating mean percentage E-rosetting lymphocytes. Elevation in the level of soluble immune **complexes** was observed to correlate closely with the presence of serum E-rosette inhibitory substance and with a diminished percentage of E-rosetting lymphocytes. There was no significant correlation between the percentage of circulating E-rosetting lymphocytes and the serum alpha 1 antitrypsin, alpha 2 macroglobulin or C-reactive protein levels. It is suggested that at high serum concentrations soluble immune **complexes** may bind selectively to human T lymphocytes in vivo, thereby inhibiting the latter's ability to form E-rosettes in vitro.

L17 ANSWER 24 OF 26 MEDLINE on STN
86007059. PubMed ID: 2412965. Control of lipopolysaccharide-high-density lipoprotein interactions by an acute-phase reactant in human serum. Tobias P S; McAdam K P; Soldau K; Ulevitch R J. Infection and immunity, (1985 Oct) 50 (1) 73-6. Journal code: 0246127. ISSN: 0019-9567. Pub. country: United States. Language: English.

AB We have recently described several phenomena involving the interactions of lipopolysaccharides (LPS) from Salmonella minnesota Re595 (Re595-LPS) with rabbit serum, which are different in and unique to acute-phase serum as compared with normal serum (P.S. Tobias and R.J. Ulevitch, J. Immunol. 131:1913-1916, 1983). To determine whether these phenomena could also be observed in acute-phase human serum (APHS), we used APHS obtained from volunteers injected with etiocholanolone. As observed in acute-phase rabbit serum, we found that (i) in APHS, Re595-LPS forms a protein **complex** with a density of 1.3 g/cm3 which does not form in normal human serum (NHS), (ii) in APHS, the t1/2 for LPS-high-density lipoprotein (HDL) complexation is at least a factor of 10 slower than the t1/2 for LPS-HDL complexation in NHS, (iii) when Re595-LPS serum mixtures are dialyzed against a low salt buffer, Re595-LPS precipitates in less soluble form from APHS than from NHS, and (iv) the precipitate from Re595-LPS-APHS mixtures includes a protein with a molecular weight of approximately 60,000 which does not precipitate from Re595-LPS-NHS mixtures or from NHS or APHS alone. These indications of an altered status of LPS in NHS and APHS suggest that one or more acute-phase reactants interact with Re595-LPS to modify its rate of binding to HDL.

L17 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
1983:573840 Document No. 99:173840 Control of lipopolysaccharide-high density lipoprotein binding by **acute phase protein**(s). Tobias, Peter S.; Ulevitch, Richard J. (Res. Inst., Scripps Clin., La Jolla, CA, 92037, USA). Journal of Immunology, 131(4), 1913-16 (English) 1983. CODEN: JOIMA3. ISSN: 0022-1767.

AB When Salmonella minnesota R595 lipopolysaccharide (LPS) is mixed with serum, the LPS eventually forms a **complex** with high d. lipoprotein (HDL). The half-life for LPS binding to HDL from normal rabbit serum (NRS) is 2-3 min. With HDL from acute phase rabbit serum (APRS; collected 24 h postinduction with AgNO3), the half-life for LPS binding to HDL is typically 40-100 min. Thus, LPS binding to HDL occurs some 20-40-fold slower in APRS than in NRS. Two other phenomena were found, the time dependencies of which correlate well with the time dependency of LPS binding to HDL in APRS. If LPS-APRS reaction mixts. are cooled to 4° shortly after mixing and are dialyzed against 2.5 mM HEPES, 15 mM NaCl, pH 7.4 buffer, LPS is recovered in the washed ppts. (euglobulin precipitate) if, and only if, the LPS-HDL binding reaction is not complete. The amount of LPS in the precipitate correlates well with the amount of LPS that has not bound to HDL. The second phenomenon observed is that the LPS-containing euglobulin precipitate prepared from LPS-acute phase serum reaction mixts. shortly after mixing also contains a protein, gp60, the concentration of which in the euglobulin precipitate correlates well with the amount of LPS in the precipitate Thus, 3 phenomena are kinetically well correlated in APRS: the degree of binding of LPS to HDL, the degree of appearance of LPS in a euglobulin fraction, and the concentration of protein gp60 in the euglobulin fraction. Glycoprotein gp60 could not be precipitated from APRS in the absence of LPS, from APRS after the LPS has fully bound to HDL, or from normal serum in the presence or absence of LPS. The known properties of gp60 are not reminiscent of any other known acute phase reactant. Thus, APRS contains acute phase reactants that interact with LPS to modify its buoyant d., its solubility, and the rate of its binding to HDL.

L17 ANSWER 26 OF 26 MEDLINE on STN
82127713. PubMed ID: 6173887. Quantitative changes of some rat proteins by short and long time carbon tetrachloride administration. Schade R; Rex H; Friedrich A. Die Pharmazie, (1981 Dec) 36 (12) 841-3. Journal code: 9800766. ISSN: 0031-7144. Pub. country: GERMANY, EAST: German Democratic Republic. Language: English.

AB In the last few years, the immunological quantitation of human plasma

proteins has proved a useful diagnostic routine method and is used in many laboratories. It is conceivable that **complex** estimations of serum proteins provide valuable and addition information on substance activities also in toxicological animal experiments. To test the validity of this concept, we have estimated the serum concentration of four proteins (IgG, transferrin, alpha2-**acute phase protein** = alpha2-AP, very low density lipoprotein = VLDL) in carbon tetrachloride-treated rats. The serum concentrations of the examined proteins are changed significantly within the first 3 d after onset of treatment. IgG and transferrin are elevated during the whole period of treatment, VLDL falls after only 1 d of treatment, and alpha2-AP shows a biphasic course. Our results are comparable with the findings described for human hepatitides. Furthermore, age-dependent and chrono-biological influences were observed.

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=> s diagnosis
L18    4513702 DIAGNOSIS

=> s l18 and blood sample
SAMPLE IS IGNORED AS A SCOPE FOR THIS SEARCH
SAMPLE IS IGNORED AS A SCOPE FOR THIS SEARCH
SAMPLE IS IGNORED AS A SCOPE FOR THIS SEARCH
SAMPLE IS IGNORED AS A SCOPE FOR THIS SEARCH
SAMPLE IS IGNORED AS A SCOPE FOR THIS SEARCH
L19     702844 L18 AND BLOOD

=> s l19 and precipitate
L20        882 L19 AND PRECIPITATE

=> s l20 and complex
L21        161 L20 AND COMPLEX

=> s l21 and lipoprotein
L22         14 L21 AND LIPOPROTEIN

=> dup remove l22
PROCESSING COMPLETED FOR L22
L23          10 DUP REMOVE L22 (4 DUPLICATES REMOVED)

=> d l23 1-10 cbib abs

L23  ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2004 ACS on STN
2002:833421   Document No. 137:322300  Direct serum lipids assays for
     evaluation of disease states.  Purdie, Neil; Krouse, Justin A.; Studer,
     Joe; Marais, Adrian D. (USA).  U.S. Pat. Appl. Publ. US 2002160519 A1
     20021031, 22 pp.  (English).  CODEN: USXXCO.  APPLICATION: US 2002-68305
     20020205.  PRIORITY: US 2001-PV266541 20010205.
AB   The invention presents a method designed to simultaneously measure certain
     unsatd. lipids and certain vitamins present either as single substances or
     in complex mixts. such as exist in serum and natural oils.
     Target lipids are free cholesterol, unsatd. cholesteryl esters; free
     polyunsatd. fatty acids, and their esters as triglycerides, and
     phospholipids.  Distributions of these analytes over the broad range of
     serum lipoproteins from chylomicrons to high d. fractions are
     determined using a procedure that involves a single step reaction in which the
     mol. unsaturations are subjected to non-enzymic color inducing reagents.
     For natural oils and vitamins, the same method serves as a quality control
     procedure.  Anal. detection is achieved using broad spectrum absorbance
     and/or fluorescence measurements.  Measured spectra are aggregates of the
     absorbance contributions from each of the analytes.  Data analyses follow
     two paths.  One uses raw spectral data.  In the other, multivariate
     methods of anal., particularly principal component (or factor) anal.,
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leads to 2-D and 3-D clustering correlations which have significant diagnostics capabilities for the early detection of human serum disorders and for quality control.

L23 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 1
2002496203. PubMed ID: 12239165. Biphasic transmittance waveform in the APTT coagulation assay is due to the formation of a Ca(++)-dependent **complex** of C-reactive protein with very-low-density **lipoprotein** and is a novel marker of impending disseminated intravascular coagulation. Toh Cheng Hock; Samis John; Downey Colin; Walker John; Becker Lev; Brufatto Nicole; Tejidor Liliana; Jones Greg; Houdijk Wim; Giles Alan; Koschinsky Marlys; Ticknor Larry O; Paton Ray; Wenstone Richard; Nesheim Michael. (Departments of Biochemistry and Pathology, Queen's University, Kingston, ON, Canada.) Blood, (2002 Oct 1) 100 (7) 2522-9. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB A decrease in light transmittance before clot formation, manifesting as a biphasic waveform (BPW) pattern in coagulation assays, was previously correlated with the onset of disseminated intravascular coagulation (DIC). In this study of 1187 consecutive admissions to the intensive care unit, the degree of this change on admission predicts DIC better than D-dimer measurements. Additionally, the BPW preceded the time of DIC **diagnosis** by 18 hours, on average, in 56% (203 of 362) of DIC patients. The BPW is due to the rapid formation of a **precipitate** and coincident turbidity change on recalcification of plasma. The isolated **precipitate** contains very-low-density **lipoprotein** (VLDL) and C-reactive protein (CRP). The addition of CRP and Ca(++) to normal plasma also causes the precipitation of VLDL and IDL, but not LDL or HDL. The K(d) of the CRP/VLDL interaction is 340 nM, and the IC(50) for Ca(++) is 5.0 mM. In 15 plasmas with the BPW, CRP was highly elevated (77-398 microg/mL), and the concentration of isolated VLDL ranged from 0.082 to 1.32 mM (cholesterol). The turbidity change on recalcification correlates well with the calculated level of the CRP-VLDL **complex**. Clinically, the BPW better predicts for DIC than either CRP or triglyceride alone. The **complex** may have pathophysiological implications because CRP can be detected in the VLDL fraction from sera of patients with the BPW, and the VLDL fraction has enhanced prothrombinase surface activity. The **complex** has been designated **lipoprotein** complexed C-reactive protein.

L23 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
1995:916448 Document No. 123:314548 Preparation of peptides containing a phosphine group for marking with 99mTc and 186-188Re or paramagnetic agents.. Mazzi, Ulderico; Lunghi, Fabio (Sorin Biomedica S.p.A., Italy). Eur. Pat. Appl. EP 659764 A2 19950628, 16 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1994-120079 19941219. PRIORITY: IT 1993-TO974 19931221.

AB R1R2P-A-B [R1, R2 = H, OH, alkoxy, PhO, (substituted) alkyl, substituted Ph; A = alkylenecarbonyl, alkyleneamino; when A = alkylenecarbonyl, then B = NHCHR3CONHCH(COZ)R4; R3 = amino acid side chain; R4 = H, alkyl, PhCH2, aminoalkyl, aminocarbonylalkyl, etc.; Z = OH, OMe, NH2, R4, peptide with biol. properties useful for **diagnosis**, radiotherapy, or magnetic resonance; when A = alkyleneamino, then B = COCHR3NHCOCHZR4, COCH2CH(COZ)NHCOCHR3NHY, COCHR3NHCO(CH2)nPR1R2; n = 1, 2; Y = H, R1R2P(CH2)nCO], were prepared Thus, H-Gly-Cys(Bzl)-OMe.HCl (preparation given) in dioxane was treated with Et3N and the resulting **precipitate** of Et3N.HCl was removed by filtration. The resulting solution was treated with Ph2PCH2CH2COOSu (Su = succinimidyl) (preparation given) to give 76% Ph2PCH2CH2CO-Gly-Cys(Bzl)-OMe.

L23 ANSWER 4 OF 10 MEDLINE on STN DUPLICATE 2
96352971. PubMed ID: 8749274. Diagnostic value of immune cholesterol as a

marker for atherosclerosis. Orekhov A N; Kalenich O S; Tertov V V; Perova N V; Novikov IyD; Lyakishev A A; Deev A D; Ruda MYa. (Institute of Experimental Cardiology, Cardiology Research Center, Moscow, Russia.) Journal of cardiovascular risk, (1995 Oct) 2 (5) 459-66. Journal code: 9436980. ISSN: 1350-6277. Pub. country: ENGLAND: United Kingdom. Language: English.

AB BACKGROUND: The serum of patients with coronary atherosclerosis contains circulating immune **complexes** including low-density **lipoproteins** (LDLs). We have developed a technique for the evaluation of LDL content in circulating immune **complexes** by measuring total cholesterol levels in polyethylene glycol **precipitates** (immune cholesterol). In the present study, the value of immune cholesterol in the **diagnosis** of atherosclerosis was compared with that of other laboratory parameters, such as total cholesterol levels, triglycerides, LDL cholesterol, high-density **lipoprotein** cholesterol, **lipoprotein**(a), and apolipoproteins B and A-1. METHODS: Immune cholesterol and the other parameters were determined in **blood** samples from 200 patients with documented coronary and extracoronary atherosclerosis. Coronary atherosclerosis was assessed by coronary angiography; stenoses in the aortic arch and branches and in lower-limb arteries were evaluated by angiography and ultrasonography. RESULTS: Only immune cholesterol and the ratio of apolipoprotein B to apolipoprotein A-1 correlated significantly with the severity of coronary atherosclerosis. The accuracy of the **diagnosis** of coronary atherosclerosis by immune cholesterol was 78%, considerably higher than that of other laboratory parameters. Use of a combined parameter consisting of immune cholesterol, LDL cholesterol, and the patient's age increased the diagnostic accuracy to 81%. A high level of immune cholesterol is characteristic not only of coronary atherosclerosis but also of extracoronary atherosclerosis. The sensitivity, specificity and accuracy of the **diagnosis** of extracoronary atherosclerosis were even higher than those for coronary atherosclerosis. CONCLUSION: Immune cholesterol may be employed as a novel marker in the **diagnosis** of advanced atherosclerosis.

L23 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

1989:190432 Document No. 110:190432 Method of differential analysis of lipid metabolism of patients suffering from heart ischemia. Kanskaya, N. V.; Karpov, R. S. (All-Union Cardiological Research Center, Tomsk, USSR). U.S.S.R. SU 1425547 A1 19880923 From: Otkrytiya, Izobret. 1988, (35), 171. (Russian). CODEN: URXXAF. APPLICATION: SU 1985-3965395 19851010.

AB For differential **diagnosis** of disorders of lipid metabolism in patients with ischemic heart disease, the serum levels of cholesterol and triacetylglycerides (sic) are determined by electrophoresis in **ppts.** of immune **complexes**. With a cholesterol level of 0.3-2.1 mM, type IIa dyslipoproteinemia is diagnosed; with a triacetylglyceride level of 0.1-0.9 mM, type IV is diagnosed; and with both levels in these ranges simultaneously, type IIb dyslipoproteinemia is diagnosed.

L23 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

1988:471415 Document No. 109:71415 Gamma-glutamyltranspeptidase isoenzyme forms and **lipoproteins** in normal and pathological sera. Castaldo, G.; Fortunato, G.; Salvatore, F.; Sacchetti, L. (II Fac. Med. Chir., Univ. Napoli, Naples, Italy). Italian Journal of Biochemistry, 37(2), 111-18 (English) 1988. CODEN: IJBIAC. ISSN: 0021-2938.

AB The mol. nature of serum γ-glutamyltranspeptidase isoenzymes [(GGT) from normal subjects and from patients affected by various hepatobiliary diseases)] was studied by selective **lipoprotein** precipitation Some fractions co-**precipitate** with low-d. **lipoprotein** (LDL) + very-low-d.**lipoprotein** (VLDL) (pre-β-, β-, β/γ-, γ-, and dep-GGT fractions) or with high- d. **lipoprotein** (HDL) (partial precipitation of α1-GGT in cirrhosis). α1-GGT + α2-GGT in normal subjects and Alb-GGT did not

precipitate with either of the precipitation treatments. Total GGT and its isoenzymes were stable at 4° and at -20° for at least 20 days, with the exception of Alb-GGT which at -20° decreased by 20%. The percentage of GGT associated with LDL + VLDL appeared to be a possible marker to discriminate liver tumors from cirrhosis. A cut-off value of 20 units/L of this marker yielded a diagnostic sensitivity of 87% and a diagnostic specificity of 85%.

L23 ANSWER 7 OF 10 EMBASE
on STN
86175217 EMBASE Document No.: 1986175217. A new form of coagulation factor VII in plasma. Dalaker K.; Skartlien A.H.; Prydz H.. Research Institute for Internal Medicine, University of Oslo, Rikshospitalet, 0027 Oslo 1, Norway. Scandinavian Journal of Haematology 36/5 (430-438) 1986. CODEN: SJHAAQ. Pub. Country: Denmark. Language: English.

AB We have reported the existence of a novel form of coagulation factor VII - probably a factor VII-phospholipid **complex** - in plasma from pregnant women and men at risk for cardiovascular disease. We report here further observations on the presence and characteristics of this **complex**. Some apparently healthy individuals who, on testing by standard methods, have normal levels of factor VII activity achieve such levels by means of a phospholipase C-sensitive modification of (some of) their factor VII molecules. Their residual factor VII activity after phospholipase C treatment of plasma may be as low as 10-20 U/ml. Antiserum to the protein component of thromboplastin (apoprotein III) had no effect on the factor VII activity, whereas antiserum to factor VII effectively blocked both the total factor VII activity and the residual activity of factor VII after treatment of plasma with phospholipase C. These factor VII **complexes precipitate** with the VLDL/LDL fraction in **lipoprotein** precipitations.

L23 ANSWER 8 OF 10 MEDLINE on STN
84241101. PubMed ID: 6429242. Preparation and characterization of monoclonal antibodies recognizing three distinct differentiation antigens (BL1, BL2, BL3) on human B lymphocytes. Wang C Y; Azzo W; Al-Katib A; Chiorazzi N; Knowles D M 2nd. Journal of immunology (Baltimore, Md. : 1950), (1984 Aug) 133 (2) 684-91. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We report in this paper the generation and characterization of three monoclonal antibodies, designated alpha BL1, alpha BL2, and alpha BL3, that recognize distinctive antigens unrelated to complement, Fc, and mouse erythrocyte rosette receptors, which are preferentially expressed on B lymphocytes. alpha BL1 recognizes a heat stable nonimmunoprecipitable antigen, possibly glycolipid in nature. Alpha BL2 recognizes a nonreducible single polypeptide with a m.w. of 68,000 that occasionally co-**precipitates** with a p29,34 **complex** of HLA-DR antigens. Alpha BL3 recognizes a nonreducible single polypeptide with a m.w. of 105,000 with an acidic pI point. We demonstrated that BL1 is expressed on fetal liver hematopoietic cells, a small subset (5 to 15%) of Ficoll-Hypaque-separated normal bone marrow cells, and on a subpopulation of nonadherent, non-E rosette-forming cells and granulocytes. BL2 is expressed on fetal liver hematopoietic cells, on 3 to 7% of normal bone marrow cells, and on a majority (40 to 70%) of nonadherent, non-E rosette-forming cells with a distinctive pattern similar to that of HLA-DR. BL3 is expressed on a subpopulation of nonadherent, non-E rosette-forming cells, and on occasional cells in the monocyte-enriched adherent cell population. The peak fluorescence for BL2 is substantially higher than that of BL1 and BL3, indicating higher BL2 antigen density. All three antigens are absent from thymocytes and E rosette-positive T cell fractions obtained from various lymphoid tissues. Cellular distribution of the BL antigens on various well-characterized established hematopoietic cell lines, leukemias, and malignant lymphomas, in conjunction with the results of the in vitro activation and TPA-induction

experiments, suggest that BL1 is expressed during early developmental stages of B cell differentiation, whereas BL3 is expressed at the later stages. BL2 expression spans immature and mature stages of B cell differentiation, with the exception of mature plasma cells. The alpha BL antibodies described here should prove to be useful in the investigation of B cell differentiation and in the clinical **diagnosis** of lymphoid neoplasms.

L23 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
1977:482511 Document No. 87:82511 Serum lipids and precipitation test of beta-**lipoproteins** in patients with ischemic heart disease and healthy controls. Waich, Salvador; Quintero, Gaudy; Camejo, German; Acquatella, Harry; Lalaguna, Fernando; Berrizbeitia, Maria Luisa (Serv. Cardiol., Hosp. Cent. Fuerzas Armadas "Carlos Arvelo", Caracas, Venez.). Acta Cientifica Venezolana, 28(1), 89-93 (Spanish) 1977. CODEN: ACVEAV. ISSN: 0001-5504.

AB The levels of serum cholesterol and triglycerides and the β-**lipoprotein** (low-d. **lipoproteins**, LDL) precipitation test, were determined in 295 cases, 55 with **diagnosis** of acute coronary heart disease, 112 with chronic ischemic heart disease and 128 healthy controls. The cholesterol of women with acute and chronic coronary heart disease is higher than that of men and healthy women but the level of serum cholesterol is the same in male groups. Higher serum triglyceride levels are more frequent in patients with chronic ischemic heart disease than in the control group. Male patients with acute coronary heart disease have a tendency to **precipitate** LDL more than the female patients, but the opposite occurs in patients with chronic ischemic heart disease. The high results of the LDL precipitation test in patients with acute and chronic ischemic heart disease suggest changes in composition of the LDL lipid components, possibly due to dietetic factors which facilitate their tendency to associate and to form insol. **complexes** with the arterial factor.

L23 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
1967:419597 Document No. 67:19597 A specific property of the plasmocytoma serum paraprotein lipids with respect to lipid precipitation by heparin. Keler-Bacoka, Mira (Univ. Hosp., Zagreb, Yugoslavia). Clinica Chimica Acta, 16(3), 365-9 (English) 1967. CODEN: CCATAR. ISSN: 0009-8981.

AB Sera from 15 patients with β- and γ-plasmocytoma, 1 serum from a patient with Waldenstroem macroglobulinemia and 12 control sera were examined in the native state and after treatment with heparin for precipitation of the β- **lipoproteins**. Contrary to the controls, all the pathologic sera showed a sharp protein-lipid (PL) band on the electrophoretic lipidogram even after removal of the β-**lipoproteins** with heparin. This finding suggests that the PL fraction cannot form insol. **complexes** with heparin. All sera were simultaneously examined by Ouchterlony double-diffusion immunopptn. The results proved that the paraprotein lipid component possesses specific antigenic properties, and, although it has the same electrophoretic mobility as the β- **lipoproteins**, it does not **precipitate** with the specific anti-β- **lipoprotein** serum. These characteristic properties of the paraprotein lipid fraction, with regard to heparin precipitation allow for a good separation of the PL fraction from the β- **lipoproteins**. The technique can be useful in **diagnosis** and in the anal. of paraprotein lipids.

=> sl21 and acute phase protein
SL21 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter

"HELP COMMANDS" at an arrow prompt (=>).

=> s l21 and acute phase protein
L24 3 L21 AND ACUTE PHASE PROTEIN

=> dup remove l24
PROCESSING COMPLETED FOR L24
L25 1 DUP REMOVE L24 (2 DUPLICATES REMOVED)

=> d l25 cbib abs

L25 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
96413703. PubMed ID: 8816857. Identification of **acute-phase proteins** (APP) in circulating immune **complexes** (CIC) in esophageal cancer patients' sera. Croce M V; Segal-Eiras A. (Centro de Investigaciones Inmunologicas Basicas y Aplicadas (CINIBA), Facultad de Ciencias Medicas, Universidad Nacional de La Plata, Argentina.) Cancer investigation, (1996) 14 (5) 421-6. Journal code: 8307154. ISSN: 0735-7907. Pub. country: United States. Language: English.

AB The occurrence of increased circulating immune **complexes** (CIC) in sera of patients with esophageal cancer and their usefulness for **diagnosis** and prognosis have not been demonstrated. Circulating **acute-phase proteins** (APP) related to esophageal cancer have been described but without any association with CIC. This is a study to measure CIC, C-reactive protein (CRP), and alpha 1-acidic glycoprotein (AAG) in pretreatment esophageal cancer sera and to analyze the presence of both APP associated with these CIC. Increased CIC levels were found in 57% of sera from esophageal cancer patients; elevated CRP was detected in 87% and AAG in 47%. Western blot analysis showed the presence of CRP and AAG in CIC-derived fractions. We conclude that: (1) CIC, CRP, and AAG are elevated in esophageal cancer sera; (2) they may be considered possible useful clinical parameters in pretreatment esophageal cancer patients; (3) these APPs appear in CIC **precipitates** and may possibly be involved in their composition.

=> s l21 and acute phase proteins
L26 3 L21 AND ACUTE PHASE PROTEINS

=> dup remove l26
PROCESSING COMPLETED FOR L26
L27 1 DUP REMOVE L26 (2 DUPLICATES REMOVED)

=> d l27 cbib abs

L27 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
96413703. PubMed ID: 8816857. Identification of **acute-phase proteins** (APP) in circulating immune **complexes** (CIC) in esophageal cancer patients' sera. Croce M V; Segal-Eiras A. (Centro de Investigaciones Inmunologicas Basicas y Aplicadas (CINIBA), Facultad de Ciencias Medicas, Universidad Nacional de La Plata, Argentina.) Cancer investigation, (1996) 14 (5) 421-6. Journal code: 8307154. ISSN: 0735-7907. Pub. country: United States. Language: English.

AB The occurrence of increased circulating immune **complexes** (CIC) in sera of patients with esophageal cancer and their usefulness for **diagnosis** and prognosis have not been demonstrated. Circulating **acute-phase proteins** (APP) related to esophageal cancer have been described but without any association with CIC. This is a study to measure CIC, C-reactive protein (CRP), and alpha 1-acidic glycoprotein (AAG) in pretreatment esophageal cancer sera and to analyze the presence of both APP associated with these CIC. Increased CIC

levels were found in 57% of sera from esophageal cancer patients; elevated CRP was detected in 87% and AAG in 47%. Western blot analysis showed the presence of CRP and AAG in CIC-derived fractions. We conclude that: (1) CIC, CRP, and AAG are elevated in esophageal cancer sera; (2) they may be considered possible useful clinical parameters in pretreatment esophageal cancer patients; (3) these APPs appear in CIC **precipitates** and may possibly be involved in their composition.

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=> d his

     (FILE 'HOME' ENTERED AT 09:26:04 ON 09 MAR 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 09:26:17 ON
     09 MAR 2004
L1           575 S CRP COMPLEX
L2             3 S L1 AND LIPOPROTEINS
L3             2 DUP REMOVE L2 (1 DUPLICATE REMOVED)
L4            50 S C REACTIVE PROTEIN COMPLEX
L5            50 S L4 AND COMPLEX
L6             0 S L5 AND LDL
L7             3 S L5 AND LIPOPROTEINS
L8             3 DUP REMOVE L7 (0 DUPLICATES REMOVED)
L9             0 S HAEMOSTATIC DYSFUNCTION DIAGNOSIS
L10            0 S LIPOPROTEIN COMPLEX RISK ASSESMENT
L11            1 S ACUTE PHASE PROTEIN COMPLEX
L12        17217 S ACUTE PHASE PROTEIN
L13            0 S L12 AND RISK ASSESMENT
L14            0 S L12 AND ASSESMENT
L15         1383 S L12 AND COMPLEX
L16           35 S L15 AND LIPOPROTEINS
L17           26 DUP REMOVE L16 (9 DUPLICATES REMOVED)
L18      4513702 S DIAGNOSIS
L19       702844 S L18 AND BLOOD
L20          882 S L19 AND PRECIPITATE
L21          161 S L20 AND COMPLEX
L22           14 S L21 AND LIPOPROTEIN
L23           10 DUP REMOVE L22 (4 DUPLICATES REMOVED)
L24            3 S L21 AND ACUTE PHASE PROTEIN
L25            1 DUP REMOVE L24 (2 DUPLICATES REMOVED)
L26            3 S L21 AND ACUTE PHASE PROTEINS
L27            1 DUP REMOVE L26 (2 DUPLICATES REMOVED)

=> s l20 and no fibrin polymerization
L28            0 L20 AND NO FIBRIN POLYMERIZATION

=> s l19 and metal ion
L29          114 L19 AND METAL ION

=> s l29 and calcium
L30           15 L29 AND CALCIUM

=> s l30 and complex
L31            2 L30 AND COMPLEX

=> dup remove l31
PROCESSING COMPLETED FOR L31
L32            2 DUP REMOVE L31 (0 DUPLICATES REMOVED)

=> d l32 1-2 cbib abs

L32  ANSWER 1 OF 2  EMBASE  COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
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95324716 EMBASE Document No.: 1995324716. A toxicologic risk for using manganese **complexes**? A literature survey of existing data through several medical specialties. Misselwitz B.; Muhler A.; Weinmann H.-J.. FKK, Schering AG, Mullerstrasse 178,D-13342 Berlin, Germany. Investigative Radiology 30/10 (611-620) 1995.
ISSN: 0020-9996. CODEN: INVRAV. Pub. Country: United States. Language: English. Summary Language: English.

AB This article summarizes data from the literature about biologic functions, toxicity, and biokinetics of manganese to help the reader assess the importance of **complex** stability of manganese-based contrast agents. Free manganese may present a greater risk than free gadolinium, especially because it has a physiologic role and can therefore trigger multiple functions. Of particular interest are the deleterious effects of manganese on the central nervous system (it can cross the intact **blood**-brain barrier) and on developing life (it penetrates the placental barrier as well and is teratogenic). After intravenous contrast injection, normal (enteral) regulation mechanisms for manganese homeostasis are bypassed, and there is a danger of individual overdosing. Excess manganese, for example in patients with chronic liver disease or with chronic parenteral nutrition, has already been detected by magnetic resonance imaging in the basal ganglia and was found to coincide with neurologic symptoms. Decomplexation with release of free manganese substantially prolongs the elimination of the metal because manganese can be excreted only slowly via the biliary system. This may be of particular importance in patients with impaired hepatic function. Although minimal amounts of free manganese ions are not considered harmful to the human body, significant decomplexation of manganese **complexes** will require careful analysis of the diagnostic benefit versus the potential risk posed by the free **metal ions**.

L32 ANSWER 2 OF 2 EMBASE
on STN

86211578 EMBASE Document No.: 1986211578. Binding of coagulation factor XI to washed human platelets. Greengard J.S.; Heeb M.J.; Ersdal E.; et al.. Department of Immunology, Scripps Clinic and Research Foundation, La Jolla, CA 92037, United States. Biochemistry 25/13 (3884-3890) 1986.
CODEN: BICHAW. Pub. Country: United States. Language: English.

AB The binding of human coagulation factor XI to washed human platelets was studied in the presence of zinc ions, **calcium** ions, and high molecular weight kininogen. Significant factor XI binding occurred at physiological levels of these **metal ions** when high molecular weight kininogen was present. Binding required platelet stimulation and was specific, reversible, and saturable. Scatchard analysis of the binding yielded approximately 1500 binding sites per platelet with an apparent dissociation constant of approximately 10 nM. Since the concentration of factor XI in plasma is about 25 nM, this suggests that in plasma factor XI binding sites on stimulated platelets might be saturated. **Calcium** ions and high molecular weight kininogen acted synergistically to enhance the ability of low concentrations of zinc ions to promote factor XI binding. The similarity between the concentrations of **metal ions** optimal for factor XI binding and those optimal for high molecular weight kininogen binding, as well as the ability of high molecular weight kininogen to modulate these **metal ion** effects, implies that factor XI and high molecular weight kininogen may form a **complex** on the platelet surface as they do in solution and on artificial negatively charged surfaces.

=> dup remove l29
PROCESSING COMPLETED FOR L29
L33 104 DUP REMOVE L29 (10 DUPLICATES REMOVED)

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=> s l33 and clot inhibitor
L34             0 L33 AND CLOT INHIBITOR

=> s l33 and acute phase proteins
L35             0 L33 AND ACUTE PHASE PROTEINS

=> s l33 and lipoproteins
L36             2 L33 AND LIPOPROTEINS

=> dup remove l36
PROCESSING COMPLETED FOR L36
L37             2 DUP REMOVE L36 (0 DUPLICATES REMOVED)

=> d l37 1-2 cbib abs

L37  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
1999:405175  Document No. 131:41829  Determination of LDL-triglycerides from
     blood using selective solubilization with cyclodextran and
     triblock copolymer.  Wieland, Heinrich; Nauck, Matthias (Germany).  PCT
     Int. Appl. WO 9931512 A1 19990624, 29 pp.  DESIGNATED STATES: W:  JP, US;
     RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
     SE.  (German).  CODEN: PIXXD2.  APPLICATION: WO 1998-EP8253 19981216.
     PRIORITY: DE 1997-19756255 19971217.
AB   The invention concerns a homogeneous assay for measuring low-d.
     lipoprotein triglycerides from blood by cyclodextrin precipitation and
     triblock polymer solubilization, followed by enzymic treatment and
     spectrophotometric glycerol determination  Serum is treated with
     α-cyclodextrin or sulfate derivs. in the presence of two-valent
     metal ions; LDL-triglycerides are selectively
     solubilized with polyoxyethylene-polyoxypropylene blockpolymer.
     Triglycerides are cleaved with lipase or esterase; glycerol is determined in a
     spectrophotometric enzyme reaction with glycerol kinase and
     glycerol-3-phosphate dehydrogenase; sensitivity enhancing substances, e.g.
     triosephosphate isomerase and glyceraldehyde-3-phosphate dehydrogenase can
     be added.  Mol. weight of the triblock polymer is 1000-8000; the triblock
     polymer has a composition A-B-A, where A represents polyoxyethylene, B
     represents polyoxypropylene; the mol. mass ratio of B is 75-95%.  The
     invention also concerns a diagnostic kit containing the necessary components;
     it can be used for the diagnosis of vascular diseases, especially
     detecting coronary cardiac disease.

L37  ANSWER 2 OF 2     MEDLINE on STN
2000074431.    PubMed ID: 10608719.  Endothelial dysfunction, oxidation of
     low-density lipoprotein, and cardiovascular disease. Holvoet P. (Center
     for Molecular and Vascular Biology, University of Leuven, Belgium..
     paulholvoet@med.kuleuven.ac.be) . Therapeutic apheresis : official journal
     of the International Society for Apheresis and the Japanese Society for
     Apheresis, (1999 Nov) 3 (4) 287-93.  Ref: 30. Journal code: 9706703. ISSN:
     1091-6660. Pub. country: United States. Language: English.
AB   The oxidative modification of low-density lipoprotein (LDL) may be
     dependent or independent of lipid peroxidation.  This peroxidation may be
     initiated by metal ions, possibly in association with
     phospholipase activity or catalyzed by myeloperoxidase independent of
     metal ions.  It results in the generation of aldehydes,
     which substitute lysine residues in the apolipoprotein B-100 moiety and
     thus in the generation of oxidized LDL.  Endothelial injury, associated
     with increased production of free radicals during oxidative stress, is
     associated with increased prostaglandin synthesis and platelet
     adhesion/activation.  These processes are associated with the release of
     aldehydes, which induce the oxidative modification of LDL in the absence
     of lipid peroxidation and thus in the generation of malondialdehyde
     (MDA)-modified LDL.  We have demonstrated an association between coronary
     artery disease (CAD) and increased plasma levels of oxidized LDL.  The
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increase of circulating oxidized LDL is most probably independent of plaque instability. Indeed, plasma levels of oxidized LDL were very similar for patients with stable CAD and for patients with acute coronary syndromes. Acute coronary syndromes, however, were associated with increased release of MDA-modified LDL that was independent of the necrosis of myocardial cells. These data suggest that oxidized LDL is a marker of coronary atherosclerosis whereas MDA-modified LDL is a marker of plaque instability. Recently, a prospective study in cardiac transplant patients suggested an active role of oxidized LDL in the development of CAD. Oxidized LDL may contribute to the progression of atherosclerosis by enhancing endothelial injury by inducing foam cell generation and smooth muscle proliferation.

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=> s (fischer t?/au or downey c?/au or nesheim m?/au or samis j?/au or tejidor
l?/au or toh c?/au or walkder j?/au)
L38        5680 (FISCHER T?/AU OR DOWNEY C?/AU OR NESHEIM M?/AU OR SAMIS J?/AU
                OR TEJIDOR L?/AU OR TOH C?/AU OR WALKDER J?/AU)

=> s l38 and diagnosis
L39         399 L38 AND DIAGNOSIS

=> s l39 and time dependent measurement
L40           4 L39 AND TIME DEPENDENT MEASUREMENT

=> dup remove l40
PROCESSING COMPLETED FOR L40
L41           4 DUP REMOVE L40 (0 DUPLICATES REMOVED)

=> d l41 1-4 cbib abs
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L41 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2003:435205 Document No. 139:19321 Method for predicting an increased likelihood of antiphospholipid syndrome in a patient using phospholipids and waveform analysis. Ortel, Thomas L.; Su, Zuowei; Braun, Paul J.; **Tejidor, Liliana** (USA). U.S. Pat. Appl. Publ. US 2003104493 A1 20030605, 47 pp. (English). CODEN: USXXCO. APPLICATION: US 2002-185186 20020628. PRIORITY: US 2001-PV302261 20010629; US 2001-PV318755 20010911.

AB A method for predicting that an individual has antiphospholipid syndrome or an increased likelihood of having antiphospholipid syndrome, includes: (a) providing a test sample from an individual; (b) combining the test sample with phospholipids; (c) directing a light beam at the test sample and monitoring light scattering or transmittance over time so as to provide a **time-dependent measurement** profile; (d) determining if a value or a slope at or over a particular time in the **time-dependent measurement** profile is beyond a corresponding predetd. value or slope threshold; and if the value or slope in the **time-dependent measurement** profile is beyond the predetd. threshold, then determining that the individual has antiphospholipid syndrome or an increased risk of antiphospholipid syndrome. The phospholipids can be provided as part of a coagulation reagent, or as part of a reagent where coagulation is not activated. Confirmatory assays for particular antibodies to phospholipid binding proteins can be performed.

L41 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2002:489176 Document No.: PREV200200489176. Method for predicting the presence of haemostatic dysfunction in a patient sample. **Toh, Cheng Hock** [Inventor, Reprint author]; **Downey, Colin** [Inventor]; **Fischer, Timothy J.** [Inventor]. Liverpool, UK. ASSIGNEE: bioMerieux, Durham, NC, USA. Patent Info.: US 6429017 August 06, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 6, 2002) Vol. 1261, No. 1. http://www.uspto.gov/web/menu/patdata.htm

1. e-file.
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB A method which may be used to determine haemostatic dysfunction in a patient is carried out by (a) adding a reagent to a test sample, wherein the test sample includes at least a component of a blood sample from a patient; and then (b) measuring the formation of a precipitate due to the reaction of the test sample and the reagent, over time so as to derive a **time-dependent measurement** profile, the reagent forming a precipitate in the test sample without causing substantial fibrin polymerization.

L41 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2002:966970 Document No. 138:21824 Method for detecting a lipoprotein-acute phase protein complex and predicting an increased risk of system failure or mortality. **Fischer, Timothy J.; Downey, Colin; Nesheim, Mike; Samis, John A.; Tejidor, Liliana ; Toh, Cheng Hock;** Walker, John B. (USA). U.S. Pat. Appl. Publ. US 2002193949 A1 20021219, 47 pp., Cont.-in-part of U. S. Ser. No. 591,642, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2001-19087 20011219. PRIORITY: US 1995-477839 19950607; US 1997-859773 19970521; US 1997-1647 19971231; US 1999-244340 19990204; US 2000-591642 20000609; WO 2001-US18611 20010608.

AB A method for diagnosing a condition of a patient involves the steps of (a) adding one or more reagents to a test sample from a patient, the test samples comprising at least part of a blood sample from the patient, in order to cause formation of a complex comprising at least one acute phase protein at least one human lipoprotein, while causing substantially no fiber polymerization; (b) measuring the formation of the complex over time so as to derive a **time-dependent measurement** profile, and (c) determining a slope and/or total change in the **time-dependent measurement** profile, so as to diagnose a condition of the patient. A greater formation of the complex is correlated to increased probability of death of the patient.

L41 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
2000:553781 Document No. 133:132103 A method and apparatus for predicting the presence of hemostatic dysfunction in a patient sample. **Toh, Cheng Hock; Downey, Colin; Fischer, Timothy J.** (Akzo Nobel N.V., Neth.). PCT Int. Appl. WO 2000046603 A1 20000810, 111 pp. DESIGNATED STATES: W: AU, CA, JP, KR, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US2987 20000204. PRIORITY: US 1999-244340 19990204.

AB A method is disclosed for predicting the presence of hemostatic dysfunction. At least one **time-dependent measurement** on an unknown sample is performed and a resp. property of the sample is measured over time so as to derive a **time-dependent measurement** profile. One or more predictor variables, including initial slope, are defined which sufficiently define the data of the **time-dependent measurement** profile. A model is then derived that represents the relationship between an abnormality and a set of predictor variables. Subsequently, the model is utilized to predict hemostatic dysfunction.

=> s l39 and complex
L42 36 L39 AND COMPLEX

=> dup remove l42
PROCESSING COMPLETED FOR L42
L43 17 DUP REMOVE L42 (19 DUPLICATES REMOVED)

=> d l43 1-17 cbib abs

L43 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
2003:435205 Document No. 139:19321 Method for predicting an increased likelihood of antiphospholipid syndrome in a patient using phospholipids and waveform analysis. Ortel, Thomas L.; Su, Zuowei; Braun, Paul J.; **Tejidor, Liliana** (USA). U.S. Pat. Appl. Publ. US 2003104493 A1 20030605, 47 pp. (English). CODEN: USXXCO. APPLICATION: US 2002-185186 20020628. PRIORITY: US 2001-PV302261 20010629; US 2001-PV318755 20010911.

AB A method for predicting that an individual has antiphospholipid syndrome or an increased likelihood of having antiphospholipid syndrome, includes: (a) providing a test sample from an individual; (b) combining the test sample with phospholipids; (c) directing a light beam at the test sample and monitoring light scattering or transmittance over time so as to provide a time-dependent measurement profile; (d) determining if a value or a slope at or over a particular time in the time-dependent measurement profile is beyond a corresponding predetd. value or slope threshold; and if the value or slope in the time-dependent measurement profile is beyond the predetd. threshold, then determining that the individual has antiphospholipid syndrome or an increased risk of antiphospholipid syndrome. The phospholipids can be provided as part of a coagulation reagent, or as part of a reagent where coagulation is not activated. Confirmatory assays for particular antibodies to phospholipid binding proteins can be performed.

L43 ANSWER 2 OF 17 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
2003:906442 The Genuine Article (R) Number: 736AL. Disseminated intravascular coagulation: old disease, new hope. **Toh C H (Reprint)**; Dennis M . Royal Liverpool Univ Hosp, Haemostasis & Thrombosis Ctr, Liverpool L7 8XP, Merseyside, England (Reprint). BRITISH MEDICAL JOURNAL (25 OCT 2003) Vol. 327, No. 7421, pp. 974-977. Publisher: B M J PUBLISHING GROUP. BRITISH MED ASSOC HOUSE, TAVISTOCK SQUARE, LONDON WC1H 9JR, ENGLAND. ISSN: 0959-535X. Pub. country: England. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Disseminated intravascular coagulation has long been associated with increased mortality in patients with sepsis. An effective treatment is now available, and the authors of this review describe how improved understanding and earlier **diagnosis** could lead to targeted treatment and improved prognosis

L43 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
2002:966970 Document No. 138:21824 Method for detecting a lipoprotein-acute phase protein **complex** and predicting an increased risk of system failure or mortality. **Fischer, Timothy J.; Downey, Colin; Nesheim, Mike; Samis, John A.; Tejidor, Liliana; Toh, Cheng Hock**; Walker, John B. (USA). U.S. Pat. Appl. Publ. US 2002193949 A1 20021219, 47 pp., Cont.-in-part of U. S. Ser. No. 591,642, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2001-19087 20011219. PRIORITY: US 1995-477839 19950607; US 1997-859773 19970521; US 1997-1647 19971231; US 1999-244340 19990204; US 2000-591642 20000609; WO 2001-US18611 20010608.

AB A method for diagnosing a condition of a patient involves the steps of (a) adding one or more reagents to a test sample from a patient, the test samples comprising at least part of a blood sample from the patient, in order to cause formation of a **complex** comprising at least one acute phase protein at least one human lipoprotein, while causing substantially no fiber polymerization; (b) measuring the formation of the **complex** over time so as to derive a time-dependent measurement profile, and (c) determining a slope and/or total change in the time-dependent measurement profile, so as to diagnose a condition of the patient. A greater formation of the **complex** is correlated to increased probability of death of the patient.

L43 ANSWER 4 OF 17 MEDLINE on STN DUPLICATE 1
2002496203. PubMed ID: 12239165. Biphasic transmittance waveform in the APTT coagulation assay is due to the formation of a Ca(++)-dependent **complex** of C-reactive protein with very-low-density lipoprotein and is a novel marker of impending disseminated intravascular coagulation. **Toh Cheng Hock; Samis John; Downey Colin;** Walker John; Becker Lev; Brufatto Nicole; **Tejidor Liliana;** Jones Greg; Houdijk Wim; Giles Alan; Koschinsky Marlys; Ticknor Larry O; Paton Ray; Wenstone Richard; **Nesheim Michael**. (Departments of Biochemistry and Pathology, Queen's University, Kingston, ON, Canada.) Blood, (2002 Oct 1) 100 (7) 2522-9. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB A decrease in light transmittance before clot formation, manifesting as a biphasic waveform (BPW) pattern in coagulation assays, was previously correlated with the onset of disseminated intravascular coagulation (DIC). In this study of 1187 consecutive admissions to the intensive care unit, the degree of this change on admission predicts DIC better than D-dimer measurements. Additionally, the BPW preceded the time of DIC **diagnosis** by 18 hours, on average, in 56% (203 of 362) of DIC patients. The BPW is due to the rapid formation of a precipitate and coincident turbidity change on recalcification of plasma. The isolated precipitate contains very-low-density lipoprotein (VLDL) and C-reactive protein (CRP). The addition of CRP and Ca(++) to normal plasma also causes the precipitation of VLDL and IDL, but not LDL or HDL. The K(d) of the CRP/VLDL interaction is 340 nM, and the IC(50) for Ca(++) is 5.0 mM. In 15 plasmas with the BPW, CRP was highly elevated (77-398 microg/mL), and the concentration of isolated VLDL ranged from 0.082 to 1.32 mM (cholesterol). The turbidity change on recalcification correlates well with the calculated level of the CRP-VLDL **complex**. Clinically, the BPW better predicts for DIC than either CRP or triglyceride alone. The **complex** may have pathophysiological implications because CRP can be detected in the VLDL fraction from sera of patients with the BPW, and the VLDL fraction has enhanced prothrombinase surface activity. The **complex** has been designated lipoprotein complexed C-reactive protein.

L43 ANSWER 5 OF 17 MEDLINE on STN DUPLICATE 2
2002692293. PubMed ID: 12452811. Waveform analysis of clotting test optical profiles in the **diagnosis** and management of disseminated intravascular coagulation (DIC). **Toh C H;** Giles A R. (Roald Dahl Haemostasis and Thrombosis Centre, Royal Liverpool University Hospital, Liverpool, UK.. toh@liverpool.ac.uk) . Clinical and laboratory haematology, (2002 Dec) 24 (6) 321-7. Ref: 15. Journal code: 7907061. ISSN: 0141-9854. Pub. country: England: United Kingdom. Language: English.

AB Transmittance waveform charts the changes in light transmittance on standard coagulation assays, such as the prothrombin time (PT) and activated partial thromboplastin time (APTT). Analysis and characterization of these data on photo-optical coagulation analysers provides additional qualitative and quantitative information to that obtained using the clotting time alone. The most thoroughly evaluated clinical application is that of the biphasic APTT waveform with disseminated intravascular coagulation (DIC). The degree of waveform abnormality correlates directly with the severity of haemostatic dysfunction and allows for both the prediction and monitoring from non-overt to overt DIC. As its performance is simple and rapid, this provides the means for targeting therapeutic intervention to an earlier stage of DIC. The recent identification that the mechanism underlying the biphasic waveform is a **complex** that exists in vivo between C reactive protein with very low density lipoprotein, provides potentially important insights into the molecular pathogenesis of DIC. Thus, in addition to the immediate clinical utility in diagnostic practice, it has important applications as a research tool. Preliminary experience in the application of this technology to the **diagnosis** and management

of the haemophilias and the lupus anticoagulant syndrome has also provided evidence of the power and utility of waveform analysis in essentially simple clotting assays.

L43 ANSWER 6 OF 17 MEDLINE on STN DUPLICATE 3
2001564742. PubMed ID: 11666089. Myocardial infarction and the balance between fibrin deposition and removal. **Nesheim M.** (Department of Biochemistry, Queen's University, Kingston, Ontario, Canada.. nesheimm@post.queensu.ca) . Italian heart journal : official journal of the Italian Federation of Cardiology, (2001 Sep) 2 (9) 641-5. Ref: 34. Journal code: 100909716. ISSN: 1129-471X. Pub. country: Italy. Language: English.

AB When fibrin deposition and removal are properly balanced, the organism is protected from both a catastrophic loss of blood at the site of injury and the inappropriate loss of fluidity within the vascular system. When these activities are not properly balanced, however, severe bleeding or thromboses can occur. Myocardial infarction is a common and morbid consequence of the latter. The thrombin/thrombomodulin **complex** plays an essential role in regulating this balance because it generates both an anticoagulant substance, activated protein C, and an antifibrinolytic substance, activated TAFI (thrombin activatable fibrinolysis inhibitor, also known as plasma carboxypeptidase B or carboxypeptidase U). Thus, the coagulation and fibrinolytic cascades are explicitly linked by virtue of thrombin catalyzed activation of TAFI, either by the thrombin/thrombomodulin **complex** or, in the absence of thrombomodulin, by the massive amounts of thrombin generated through the factor XI-dependent pathway after clotting. Some potential targets for **diagnosis**, prognosis and therapy related to the balance between fibrin formation and removal include: development of a convenient global assay for plasma fibrinolytic potential; an assay for plasma or urine thrombomodulin that had been oxidized at methionine 388 and thereby has lost its capacity to stimulate activation of protein C but not TAFI; an assay for activated TAFI; discovery of a means for tapping the tremendous potential of the vasculature to acutely release tissue-type plasminogen activator; and an assessment of the potential role of polymorphisms in the TAFI gene which might influence TAFI levels or the properties TAFIa. In addition, a much fuller and quantitative understanding of the properties of the coagulation and tibrinolytic cascades is needed in order to optimize **diagnosis**, prognosis and therapy in disorders such as myocardial infarction that are related to the balance between fibrin formation and removal.

L43 ANSWER 7 OF 17 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
1999:933292 The Genuine Article (R) Number: 259JM. Synthesis of tumour affine Yb-169-and Y-90-porphyrin **complexes** and animal experiments with different Yb-169-porphyrins. Schomacker K (Reprint); Gaidouk M I; Rumyantseva V D; **Fischer T**; Lohr H; Salditt S; Liebenhoff S; Schicha H. UNIV COLOGNE, NUKL MED KLIN & POLIKLIN, JOSEPH STELZMANN STR 9, D-50924 COLOGNE, GERMANY (Reprint). NUKLEARMEDIZIN (20 NOV 1999) Vol. 38, No. 7, pp. 285-291. Publisher: F K SCHATTAUER VERLAG GMBH. P O BOX 10 45 43, LENZHALDE 3, D-70040 STUTTGART, GERMANY. ISSN: 0029-5566. Pub. country: GERMANY. Language: German.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Aim: It should be shown, that it is possible to insert radioactive isotopes of Yb and Y into some selected porphyrins. Besides, first informations about the biodistribution of Yb-169-por-phyrin-**complexes** should be obtained. Methods: Carrier added radioactive isotopes were used for the synthesis of the metal porphyrin **complexes**. The animal experiments were done with mamma carcinoma bearing mice. The activity of the organs was determined 5 and 24 h after i.v. injection in a well counter. Results: Four Yb-169-porphyrin **complexes** and Y-90-porphyrin **complexes** could be synthesized in non-carrier-free form. This was verified by absorption

spectra, TLC and HPLC. Depending on the **complex**, the average tumour/background ratios were between 2 and 20. Conclusion: The synthesized radioactive metal-porphyrin **complexes** showed a clear tumour-affinity wich could be used for tumour scintigraphy or perhaps therapy if the synthesis is improved (goal: reduction of carrier, other radionuclides).

L43 ANSWER 8 OF 17 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

1999194817 EMBASE Direct and non-direct measurement techniques for analysis of skin surface topography. **Fischer T.W.**; Wigger-Alberti W.; Elsner P.. Prof. P. Elsner, Department of Dermatology, Friedrich Schiller University Jena, Erfurter Strasse 35, D-07740 Jena, Germany. Skin Pharmacology and Applied Skin Physiology 12/1-2 (1-11) 1999.
Refs: 24.
ISSN: 1422-2868. CODEN: SPAPFF. Pub. Country: Switzerland. Language: English. Summary Language: English.

AB Estimation of skin smoothness is of ever-increasing interest especially in the field of cosmetic research. There are some established methods for assessing skin smoothness, e.g. optical and mechanical profilometry, but the presentation of recently developed new methods reflects the demand for alternatives which are more precise and practical. For fundamental research on ultrastructure of the stratum corneum surface scanning electron microscopy is a suitable method. A direct method is the surface evaluation of living skin, which is based on an optical system in a CCD camera measuring four parameters of roughness, scaling, smoothing and wrinkling. A similar but non-direct method is optical profilometry using skin replicas. Laser profilometry produces a variety of data which can be analysed using **complex** mathematical functions. A promising new method is transparency profilometry (skin visiometer) using a very thin skin print which allows parallel light to pass through and is analysed immediately after production. The different methods can be used for characterization of the skin microrelief in dermatoses or for dynamic measurements of time-dependent changes in skin surface topography after application of cosmetic or medical products.

L43 ANSWER 9 OF 17 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

1998156985 EMBASE Disorders of the forearm axis. Graham T.J.; **Fischer T.J.**; Hotchkiss R.N.; Kleinman W.B.. Dr. T.J. Graham, Hand/Upper Extremity Cleveland Ctr., Department of Orthopaedic Surgery, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, United States. Hand Clinics 14/2 (305-316) 1998.
Refs: 66.
ISSN: 0749-0712. CODEN: HACLEO. Pub. Country: United States. Language: English. Summary Language: English.

AB Forearm pronosupination is a **complex**, integrated activity that demands specialized function of all structures between the elbow and wrist. This article describes the forearm axis as a comprehensive concept to unify these relationships. The anatomy and biomechanics of the forearm axis are reviewed. Pathologies that affect the entire axis are summarized.

L43 ANSWER 10 OF 17 MEDLINE on STN DUPLICATE 4

97452343. PubMed ID: 9308757. Properties of optical data from activated partial thromboplastin time and prothrombin time assays. Braun P J; Givens T B; Stead A G; Beck L R; Gooch S A; Swan R J; **Fischer T J.** (Organon Teknika Corporation, Durham, North Carolina 27712, USA.) Thrombosis and haemostasis, (1997 Sep) 78 (3) 1079-87. Journal code: 7608063. ISSN: 0340-6245. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Changes in characteristics of optical transmittance data from coagulation assays were examined as a function of concentration of coagulation proteins or anticoagulants. Transmittance data were collected for

activated partial thromboplastin time (APTT) and prothrombin time (PT) assays from: 1) plasmas prepared by mixing normal plasmas with deficient plasmas to give varying levels of coagulation proteins; 2) plasmas containing added heparin; and 3) 200 specimen plasmas that were also assayed for fibrinogen, coagulation factors, and other components. Optical profiles were characterized using a set of parameters describing onset and completion of coagulation, magnitude of signal change, rate of coagulation and other properties. Results indicated that parameters other than those typically reported for APTT and PT are associated with individual deficiencies, but that **diagnosis** of specimen status on the basis of optical data is **complex**. These results suggest possibilities for expanded interpretation of PT/APTT optical data for clinical or research applications.

L43 ANSWER 11 OF 17 EMBASE
on STN

95181533 EMBASE Document No.: 1995181533. The infected nonunion of the tibia.
Toh C.-L.; Jupiter J.B.. Orthopaedic Trauma Service, Massachusetts General Hospital, 15 Parkman St,Boston, MA 02114, United States. Clinical Orthopaedics and Related Research -/315 (176-191) 1995.
ISSN: 0009-921X. CODEN: CORTBR. Pub. Country: United States. Language: English. Summary Language: English.

AB Ununited fracture of the tibia complicated by infection is not only a **complex** surgical problem but also a chronic and at times debilitating condition. The principle methods used to diagnose and stage posttraumatic tibial osteomyelitis are described. Infected nonunions of the tibia are characterized by the extent of bony loss and the presence of a functional ipsilateral fibula. Using this tibial staging criteria, a series of 37 infected nonunions of the tibia are reviewed. Twenty patients were male and 16 were female, with an average age of 33 years. The distal third of the tibia was involved in 19 patients, the middle third in 11, and proximal third in 7. Twenty three of the tibia were infected with >1 organism. Thirty were Type 3 (tibial defect of 6 cm or less with a long and usable fibula), 4 Type 4 (tibial defect >6 cm with usable fibula), and 3 Type 5 (tibial defect >6 cm without usable fibula). The patients were evaluated at an average of 61 months after treatment. Union and eradication of infection were achieved in 35 of 37 patients. The results of the Health Impact Analysis suggest that the infected nonunion of the tibia represented a chronic and debilitating disorder with a lasting impact.

L43 ANSWER 12 OF 17 MEDLINE on STN DUPLICATE 5
94314946. PubMed ID: 8040300. Studies of thrombin-induced proteoglycan release in the degradation of human and bovine cartilage.
Furmaniak-Kazmierczak E; Cooke T D; Manuel R; Scudamore A; Hoogendorn H; Giles A R; **Nesheim M.** (Department of Biochemistry, Queen's University, Kingston, Ontario, Canada.) Journal of clinical investigation, (1994 Aug) 94 (2) 472-80. Journal code: 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB Because fibrin is commonly observed within arthritic joints, studies were undertaken to determine whether purified coagulation and fibrinolytic proteases degrade cartilage in vitro and to seek evidence for the activation of coagulation in arthritic joints through measurements of the levels of inhibitor-enzyme **complexes** and several other proteins associated with coagulation and fibrinolysis. The concentrations of 13 plasma proteins and **complexes** of thrombin and Factor Xa with antithrombin III were measured in synovial fluids recovered at the time of knee replacement surgery. All zymogens necessary to constitute the coagulation cascade were present. Thrombin and the combination of prothrombin plus prothrombinase induced proteoglycan release from both normal and arthritic cartilages. Factor Xa and plasmin induced release from diseased cartilage only, and urokinase, tissue plasminogen activator, and activated protein C were without effect at the levels used. At

saturating levels of thrombin (> or = 2.0 microM) 80% of the proteoglycan content of normal cartilage was released within 24 h. Thrombin, which is cationic, reversibly binds cartilage with Kd = 7.0 +/- 1.0 microM and Bmax = 820 +/- 70 ng/mg of human cartilage. Levels of thrombin-antithrombin III **complexes** in synovial fluids and arthritis were 4-fold higher in osteo (OA) and 43-fold higher in rheumatoid (RA) than in controls (0.98 nM). Factor Xa-antithrombin III **complex** levels were threefold lower in OA and fivefold higher in RA than in controls (0.24 nM). These elevated levels of enzyme-inhibitor **complexes** imply a history of activation of coagulation within the joint, especially in RA. Since thrombin degrades cartilage in vitro and had been generated in vivo, as inferred by the existence of thrombin-antithrombin III **complexes**, intraarticular activation of coagulation may both contribute to the pathology of arthritis and comprise a target for therapy and **diagnosis**.

L43 ANSWER 13 OF 17 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 6

94086510 EMBASE Document No.: 1994086510. Plasma concentration of elastase-α1-proteinase inhibitor **complex** in surfactant-treated preterm neonates with respiratory distress syndrome. Tegtmeyer F.K.; Moller J.; Richter A.; Wilken B.; **Fischer T.**. Dept of Pediatrics, Medical University of Luebeck, Kahlhorststrasse 31-35,DW-23538, Germany. European Respiratory Journal 7/2 (260-264) 1994.
ISSN: 0903-1936. CODEN: ERJOEI. Pub. Country: Denmark. Language: English. Summary Language: English.

AB Although exogenous surfactant replacement improves respiratory distress syndrome (RDS) of immature neonates, it may not prevent subsequent lung damage and development of bronchopulmonary dysplasia associated with polymorphonuclear neutrophil (PMN)-activation. We therefore wanted to assess whether surfactant administration would be associated with activation of circulating PMNs. Since elastase-α1-proteinase inhibitor (E-α1-PI) has proved to be a sensitive indicator of intravascular PMN activation, we studied E-α1-PI plasma concentration in preterm neonates during the treatment of RDS with a bovine surfactant preparation (group I: n=23). Results were compared with those from a retrospective control group treated by ventilation alone (group II: n=13), and with a reference group of 92 newborns (group III). Following surfactant administration, median E-α1-PI concentration increased significantly (day 1 80.5 vs Day 2 234 μg · l- 1), and exceeded the upper limit of the reference range of 274 μg · l-1 in seven patients, with a maximal value of 1,881 μg · l-1 after multiple surfactant administrations. In contrast, 12 infants from Group II showed no increase in median E-α1-PI levels (Day 1 107 vs Day 2 107 μg · l-1), and remained within the reference range (Day 1 125 μg · l-1; Day 2 107 μg · l-1) of the 92 newborns without respiratory impairment, infection, birth-trauma or asphyxia. From these results, it is concluded that surfactant may trigger a transient, mainly local, inflammatory response, reflected by increased levels of E-α1-PI, and may exert a dose-related pathogenic influence on the course and prognosis of RDS. Under these conditions, the validity of E-α1-PI for the **diagnosis** of early-onset septicaemia may be limited.

L43 ANSWER 14 OF 17 MEDLINE on STN DUPLICATE 7

87236948. PubMed ID: 3591034. [Neuropathologic findings in 13 deceased patients with acquired immunologic deficiency syndrome]. Neuropathologische Befunde bei 13 Verstorbenen mit erworbenem Immundefektsyndrom. Schwenk J; Ferszt R; Gosztonyi G; Lowes P; Niedobitek G; **Fischer T**; Sommer D; Cervos-Navarro J. Zentralblatt fur allgemeine Pathologie und pathologische Anatomie, (1987) 133 (1) 29-48.
Journal code: 9105593. ISSN: 0044-4030. Pub. country: GERMANY, EAST:

German Democratic Republic. Language: German.

AB The neuropathological findings in 13 patients with the acquired immune deficiency syndrome (AIDS) and with AIDS related **complex** (ARC) are reported. Six patients presented with neurological symptoms, whereas autopsy revealed CNS involvement in nine cases. Four patients showed neither neurological nor neuropathological abnormalities. The most frequent neuropathological **diagnoses** were toxoplasma encephalitis (4 cases) and multiple or solitary cerebral necroses (3 cases). Long tract degeneration of the spinal cord was found in 2 cases. Cytomegalovirus infection, progressive multifocal leukoencephalopathy, primary lymphoma of the CNS, infiltration of the leptomeninges by plasmocytoma cells and a solitary metastasis of a bronchial carcinoma were diagnosed in one case each. Subacute leukoencephalitis, mentioned frequently in the literature, was not present in this material. In one case, however, status spongiosus and gliosis was found in the cortex and basal ganglia. As similar spongy changes can be seen in mice infected experimentally with retroviruses, a pathogenetic role of the human T-cell lymphotropic/leukaemia virus type III (HTLV-III) cannot be ruled out. Astrogliosis and hypertrophy of astrocytes were found in nine cases. Morphometrically, the number of astrocytes was significantly higher in AIDS patients than in control cases which were selected randomly on grounds of comparable age. Whether this finding bears some relationship with HTLV-III encephalopathy remains open to further investigation. Glial nodules were found in four cases; according to silver impregnation they were composed of microglial elements.

L43 ANSWER 15 OF 17 EMBASE
on STN

83035753 EMBASE Document No.: 1983035753. [Portal-vein aneurysm and hepatic fibrosis in myelofibrosis]. PFORTADERANEURYSMA UND LEBERFIBROSE BEI MYELOFIBROSE. Schmitt Graff A.; Borchard F.; Winkelmann M.; **Fischer Th. J.**. Pathol. Inst., Univ. Dusseldorf, 4000 Dusseldorf, Germany. Deutsche Medizinische Wochenschrift 107/51-52 (1969-1972) 1982. CODEN: DMWOAX. Pub. Country: Germany. Language: German. Summary Language: English.

AB In a 54-year-old woman with oesophageal varices there were the unusual morphological findings of portal-vein aneurysm and irregular hepatic fibrosis. The patient had been treated for 8 years for polycythaemia vera with transition into myelofibrosis. Histologically the hepatic tissue showed occlusion of intrahepatic portal-vein branches by organised thrombi, as well as angiomatous vessels in the sclerosed portal areas. The increased pressure as well as medial atrophy with portal-vein sclerosis were the cause of the portal-vein aneurysm. Portal hypertension may have been the result of intrahepatic vascular obstruction and of the increased flow through the enlarged spleen. It is suggested that interaction of several factors, related to the basic disease of myelofibrosis led to these **complex** anomalies of the liver and portal vascular system.

L43 ANSWER 16 OF 17 EMBASE
on STN

81010011 EMBASE Document No.: 1981010011. Identification of a congenital dysthrombin, thrombin Quick. Henriksen R.A.; Owen W.G.; **Nesheim M.E.**; Mann K.G.. Dept. Pathol., Univ. Iowa, Iowa City, Ia. 52240, United States. Journal of Clinical Investigation 66/5 (934-940) 1980. CODEN: JCINAO. Pub. Country: United States. Language: English.

AB A dysprothrombin designated prothrombin Quick, is isolated from the plasma of an individual with <2% of normal functional prothrombin activity and 34% of the normal prothrombin level by immunologic assay. With Factor Xa or taipan snake venom as activators, a fragmentation pattern identical to that of normal prothrombin is observed on gel electrophoresis in dodecylsulfate. This evidence combined with the observed barium citrate adsorption of prothrombin Quick and the low activity suggests that the defect in prothrombin Quick is in the thrombin portion of the molecule.

Thrombin Quick is isolated and comigrates with thrombin on dodecyl sulfate gel electrophoresis, either reduced or nonreduced. The activity of thrombin Quick on several biological substrates of thrombin is investigated. Relative to normal thrombin, thrombin Quick is 1/200 as active on fibrinogen and 1/20-1/50 as effective in activating Factors V and VIII and aggregating platelets. A **complex** with antithrombin III is detected by dodecyl sulfate gel electrophoresis. Further investigation with the active site titrant, dansylarginine-N-(3-ethyl-1,5-pentanediyl)amide showed that the thrombin Quick preparation has the same affinity for the titrant as thrombin, but apparently only 40% active sites per mole protein are titrable.

L43 ANSWER 17 OF 17 EMBASE
on STN

74043341 EMBASE Document No.: 1974043341. Diagnostic and therapeutic applications of semi floating electrode in the management of cardiac arrhythmias. Wan S.H.; **Toh C.C.S.**. Dept. Med., Alexandra Gen. Hosp., Singapore, Singapore. Annals of the Academy of Medicine Singapore 2/1 (18-28) 1973.
CODEN: AAMSCG. Language: English.

AB The semi floating electrode is a valuable adjunct to the diagnostic and therapeutic armament of the modern cardiologist. The intra atrial ECG helps to decipher **complex** arrhythmias, especially in atrial tachycardia with intra ventricular conduction defects versus ventricular tachycardia. Diagnostically, atrial pacing serves to evaluate sinoatrial function and expose 'concealed' junctional and infra junctional disturbances. Therapeutically, atrial pacing by the semi floating technique is life saving in the emergency management of sick sinus syndrome and for overdriving of tachyarrhythmias, whether ventricular or supra ventricular. A-V junctional disease precludes atrial pacing, and ventricular pacing could be achieved by simply 'floating' the electrode further downstream. Apart from high grade A-V block, emergency ventricular pacing is employed for 'bi nodal' disease and A-V dissociation with bradyarrhythmias. As a diagnostic procedure, the intra cardiac electrogram is superior to the esophageal lead. As a therapeutic measure, pacing by the semi floating electrode is life saving in emergency conditions; it has the advantages of versatility and speed, but it suffers from the risk of current leakage when connected to powered equipment, while electrode instability is a technical difficulty.

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